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ning of each regular issue of the PCT Gazette.*

(54) Title: PERSONAL CLEANSING COMPOSITIONS COMPRISING SILICONE RESIN-CONTAINING ADHESIVES

(57) Abstract: Disclosed are personal cleansing compositions for rinse-off application to the hair, nails or skin. These compositions comprise a silicone-resin based adhesive including a silicone resin copolymer as a condensation product of an organosiloxane fluid and a silicone resin; a cleansing surfactant; and a carrier liquid. The personal cleansing compositions can also comprise as the silicone-resin based adhesive, in addition to or in place of the silicone resin copolymer, a combination of an organosiloxane resin and a diorganosiloxane fluid at a weight ratio of said resin to said fluid of from about 1:9 to about 10:1. The personal cleansing compositions provide hair styling benefits when applied to the hair, and when applied to the skin, barrier protection from surfactants or other materials having skin irritation potential.

It is therefore an object of the present invention to provide an alternative personal cleansing composition not previously described or otherwise known in the various arts, and which provides improved delivery of a film-forming polymer to the hair, nails or skin. It is a further object of the present invention to provide a personal cleansing composition that provides a base composition that helps to eliminate or minimize skin irritation associated with the topical application of various surfactants and other materials having similar skin irritation potential.

#### **SUMMARY OF THE INVENTION**

The present invention relates to personal cleansing compositions for topical rinse-off application to the hair, nails or skin. These compositions are rinse-off formulations that comprise from about 0.05% to about 40% by weight of a silicone resin-based adhesive, wherein the adhesive includes a silicone resin copolymer as a condensation product of a diorganosiloxane fluid and an organosiloxane resin; from about 0.5% to about 30% by weight of a cleansing surfactant; and from about 20% to about 99% by weight of a carrier liquid.

The present invention also relates to personal cleansing compositions for topical rinse-off application to the hair, nails or skin, said compositions comprising from about 0.05% to about 40% by weight of a silicone-resin based adhesive, wherein the adhesive is provided by a combination of an organosiloxane resin and an organosiloxane fluid, wherein the weight ratio of the organosiloxane resin to the diorganosiloxane fluid ranges from about 1:9 to about 10:1.

It has been found that the cleansing compositions of the present invention are effective in providing styling benefits when applied to and rinsed from the hair, including hair volume reduction and other hair cosmetic benefits made possible by the deposition onto hair of the film-forming materials as defined herein.

It is also believed that the personal cleansing compositions of the present invention provide adhesive and/or film-forming benefits when applied to the skin, even though the composition is a rinse-off cleansing composition. The film forming benefits are especially useful in protecting the skin from the irritation potential of different cleansing surfactants or other ingredients that tend to be irritating to the skin. It is believed that the compositions provide effective deposition of a cosmetically desirable film onto the skin during cleansing and subsequent rinsing, that provides protection of the skin from skin irritants within and external to the cleansing composition.

All percentages, parts and ratios as used herein are by weight of the total composition, unless otherwise specified. All such weights as they pertain to listed ingredients are based on the active level and, therefore, do not include solvents or by-products that may be included in commercially available materials, unless otherwise specified.

The personal cleansing compositions of the present invention can comprise, consist of, or consist essentially of the essential elements and limitations of the invention described herein, as well as any additional or optional ingredients, components, or limitations described herein or otherwise useful in personal cleansing compositions intended for topical application to the hair, nail or skin.

#### **Product Form**

The personal cleansing compositions of the present invention can be formulated in any of a variety of product forms ranging from solids or semi-solids to liquids. The key to all of the varied product forms contemplated within the scope of the compositions of the present invention is the selected and defined combination of a film-forming material as defined herein, a liquid carrier, and a surfactant. These compositions include hair care products such as shampoos, skin cleansing or body wash compositions, hand cleansing products, and other functionally similar personal cleansing products.

All of the product forms contemplated for purposes of defining the present invention are rinse-off formulations, by which is meant the product is applied topically to the skin and then subsequently and immediately (i.e., within minutes) rinsed away with water, or otherwise wipe off using a substrate or other suitable removal means.

The compositions of the present invention are not intended for, and specifically exclude, leave-on formulations and applications.

#### **Surfactant**

The personal cleansing compositions of the present invention comprise a cleansing surfactant suitable for application to the hair, nails or skin. Suitable surfactants for use herein include any known or otherwise effective cleansing surfactant suitable for application to the hair, nails or skin, and which is otherwise compatible with the other essential ingredients in the compositions.

Surfactants suitable for use in the personal cleansing compositions of the present invention include anionic, nonionic, cationic, zwitterionic or amphoteric surfactants, or combinations thereof, at product concentrations of from about 0.5% to about 30%, more typically from about 4% to about 30%, more typically from about 5% to about 25%, by weight, of the personal

Additional examples of suitable anionic surfactants are the reaction products of fatty acids esterified with isethionic acid and neutralized with sodium hydroxide where, for example, the fatty acids are derived from coconut oil; sodium or potassium salts of fatty acid amides of methyl tauride in which the fatty acids, for example, are derived from coconut oil. Other suitable anionic surfactants of this variety are described in U.S. Patent 2,486,921, U.S. Patent 2,486,922 and U.S. Patent 2,396,278.

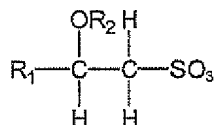
Still other suitable anionic surfactants are the succinamates, examples of which include disodium N-octadecylsulfosuccinamate; diammoniumlauryl sulfosuccinamate; tetrasodium N-(1,2-dicarboxyethyl)-N-octadecylsulfosuccinamate; diamyl ester of sodium sulfosuccinic acid; dihexyl ester of sodium sulfosuccinic acid; and dioctyl esters of sodium sulfosuccinic acid.

Other suitable anionic surfactants include olefin sulfonates having about 12 to about 24 carbon atoms. The term "olefin sulfonates" is used herein to mean compounds which can be produced by the sulfonation of  $\alpha$ -olefins by means of uncomplexed sulfur trioxide, followed by neutralization of the acid reaction mixture in conditions such that any sulfones which have been formed in the reaction are hydrolyzed to give the corresponding hydroxy-alkanesulfonates. The sulfur trioxide can be liquid or gaseous, and is usually, but not necessarily, diluted by inert diluents, for example by liquid  $\text{SO}_2$ , chlorinated hydrocarbons, etc., when used in the liquid form, or by air, nitrogen, gaseous  $\text{SO}_2$ , etc., when used in the gaseous form.

The  $\alpha$ -olefins from which the olefin sulfonates are derived are mono-olefins having about 12 to about 24 carbon atoms, preferably about 14 to about 16 carbon atoms. Preferably, they are straight chain olefins.

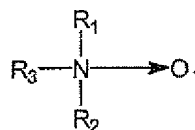
In addition to the true alkene sulfonates and a proportion of hydroxy-alkanesulfonates, the olefin sulfonates can contain minor amounts of other materials, such as alkene disulfonates depending upon the reaction conditions, proportion of reactants, the nature of the starting olefins and impurities in the olefin stock and side reactions during the sulfonation process.

Another class of anionic surfactants suitable for use in the shampoo compositions are the  $\beta$ -alkyloxy alkane sulfonates. These compounds have the following formula:



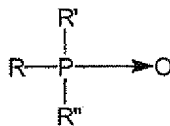
organic hydrophobic compound, which may be aliphatic or alkyl aromatic in nature. Preferred classes of nonionic surfactants include:

- 1) polyethylene oxide condensates of alkyl phenols, e.g., the condensation products of alkyl phenols having an alkyl group containing from about 6 to about 20 carbon atoms in either a straight chain or branched chain configuration, with ethylene oxide, the ethylene oxide being present in amounts equal to from about 10 to about 60 moles of ethylene oxide per mole of alkyl phenol;
- 2) nonionic surfactants derived from the condensation of ethylene oxide with the product resulting from the reaction of propylene oxide and ethylene diamine products;
- 3) condensation products of aliphatic alcohol's having from about 8 to about 18 carbon atoms, in either straight chain or branched chain configuration, with ethylene oxide, e.g., a coconut alcohol ethylene oxide condensate having from about 10 to about 30 moles of ethylene oxide per mole of coconut alcohol, the coconut alcohol fraction having from about 10 to about 14 carbon atoms;
- 4) long chain tertiary amine oxides corresponding to the following general formula:



wherein R<sub>1</sub> contains an alkyl, alkenyl or monohydroxy alkyl radical of from about 8 to about 18 carbon atoms, from 0 to about 10 ethylene oxide moieties, and from 0 to about 1 glyceryl moiety, and R<sub>2</sub> and R<sub>3</sub> contain from about 1 to about 3 carbon atoms and from 0 to about 1 hydroxy group, e.g., methyl, ethyl, propyl, hydroxyethyl, or hydroxypropyl radicals;

- 5) long chain tertiary phosphine oxides corresponding to the following general formula:



wherein R contains an alkyl, alkenyl or monohydroxyalkyl radical ranging from about 8 to about 18 carbon atoms in chain length, from 0 to about 10 ethylene oxide moieties and from 0 to about 1 glyceryl moiety and R' and R'' are each alkyl or monohydroxyalkyl groups containing from about 1 to about 3 carbon atoms;

Other zwitterionic surfactants suitable for use herein include betaines, including high alkyl betaines such as coco dimethyl carboxymethyl betaine, cocoamidopropyl betaine, cocobetaine, lauryl amidopropyl betaine, oleyl betaine, lauryl dimethyl carboxymethyl betaine, lauryl dimethyl alphacarboxyethyl betaine, cetyl dimethyl carboxymethyl betaine, lauryl bis-(2-hydroxyethyl) carboxymethyl betaine, stearyl bis-(2-hydroxypropyl) carboxymethyl betaine, oleyl dimethyl gamma-carboxypropyl betaine, and lauryl bis-(2-hydroxypropyl)alpha-carboxyethyl betaine. The sulfobetaines may be represented by coco dimethyl sulfopropyl betaine, stearyl dimethyl sulfopropyl betaine, lauryl dimethyl sulfoethyl betaine, lauryl bis-(2-hydroxyethyl) sulfopropyl betaine and the like; amidobetaines and amidosulfobetaines, wherein the  $RCONH(CH_2)_3$  radical is attached to the nitrogen atom of the betaine are also useful in this invention.

#### Liquid Carrier

The personal cleansing compositions of the present invention can be formulated in solid, semi-solid or liquid form, but must always comprise a liquid carrier suitable for topical application to the skin that is also compatible with the essential materials selected for use herein. The liquid carrier must be a liquid under ambient conditions or is otherwise in liquid form as formulated within the compositions, and helps to solubilize the film-forming material as described herein or otherwise helps to maintain the material as solubilized or in liquid form within the composition. The liquid carrier can be aqueous or anhydrous, and includes carrier liquids that are silicone-containing or non silicone-containing, volatile or non-volatile, aqueous or non-aqueous.

The personal cleansing compositions of the present invention preferably and typically comprise an aqueous carrier liquid, wherein the personal cleansing compositions preferably comprise water at a level that represents from 20% to about 98%, preferably from about 30% to about 90%, even more preferably from about 60% to about 90%, by weight of the personal cleansing compositions.

Other liquid carriers suitable for use herein, when used alone or in combination with water or other carrier liquid material, specifically excludes the organosiloxane fluids when such fluids are used in combination with an organosiloxane resin component of the composition. When the composition does not contain such silicone resin materials, then the organosiloxane fluid or other silicone containing fluids, including both volatile and non volatile silicones, are considered carrier liquids for purposes of more clearly defining the compositions of the present invention.

Volatile hydrocarbons suitable for use as a liquid carrier in the personal cleansing compositions herein include those hydrocarbons having boiling points in the range of from about

groups, alkoxy groups and mixtures thereof. Polydimethylsiloxanes are preferred, especially linear dimethicones having a viscosity of from about 5cs to about 500,000 cs, preferably from about 10 cs to about 200,000 cs, as measured at 25°C.

Other liquid carriers suitable for use herein include non-volatile esters and other similar non-volatile fluids, non-limiting examples of which include isopropyl myristate, isopropyl palmitate, and combinations thereof.

#### **Silicone Resin Copolymer**

The personal cleansing compositions of the present invention comprise a film-forming material that preferably comprises a silicone resin copolymer derived from the condensation or other functionally similar reaction or combination of an organosiloxane resin with a diorganopolysiloxane fluid. These silicone resin copolymers are known for use as adhesives in various consumers' products and applications, and are now formulated into the compositions of the present invention for the purpose of improving providing improved personal cleansing benefits as described herein.

It has been found that these silicone resin copolymers as defined herein provide effective film-forming benefits even when formulated along with a cleansing surfactant in a rinse-off formulation

The concentration of silicone resin copolymer in the topical compositions of the present invention varies considerably depending upon other ingredients in the composition as well as the intended product form. Generally, silicone resin copolymer concentrations range from about 0.05% to about 40%, preferably from about 0.1% to about 30%, more preferably from about 2% to about 20%, by weight of the topical composition. The silicone resin copolymer is preferably further selected to have an average molecular weight of at least about 15,000, more preferably at least about 15,000 to 4 million, more preferably from about 100,000 to about 3 million, although it is understood that solid silicone resin copolymers can be solubilized and formulated into the composition, wherein such solid copolymers can have an immeasurably or almost immeasurably high viscosity.

The silicone resin copolymers can for use in the compositions can be prepared by any known or otherwise effective method or chemistry for making such materials, non limiting examples of which include co-hydrolysis or by reacting triorganosilanes or other similar siloxanes with a silica h. The silicone resin copolymers are generally prepared by mixing and heating together an organosiloxane resin, diorganosiloxane fluid, and catalyst, all as described herein, at a temperature of above about 100°, until the desired adhesive character of the resulting

long as such materials are hydroxyl end blocked. The viscosity of the diorganosiloxane polymer is preferably from about 100 to about 1,000,000 cs at 25°C.

The organic amino compound for use as a catalyst in preparing the silicone resin copolymer includes any aliphatic hydrocarbon amine; alkanol amine; carboxylic acid salt thereof; and tertiary amines such as trimethylamine, tributylamine, methyldipropylamine, and quaternary ammonium salts. This includes primary amines such as hexylamine, butanolamine, and butylamine; secondary amines such as diethylamine, diethanolamine, ethylamylamine and propylhexylamine; tertiary amines such as trimethylamine, tributylamine, methyldipropylamine, tripropanolamine, and methylpropylhexylamine; and quaternary ammonium salts such as tetramethylammonium acetate and methylethyldibutylammoniumchloride, including such as the quaternary ammonium emulsifying agents sold under various trade names, such as dioctadecyldimethylammonium chloride. In addition, any carboxylic acid salt of the amines, such as diethylamine acetate, butylamine octoate and trimethylamine laurate can be used. Tertiary amines are preferred, especially tertiary aliphatic amines.

#### **Organosiloxane Resin Adhesives**

The compositions of the present invention also preferably comprise an adhesive material that contains an organosiloxane resin, wherein the resin is used in combination with a liquid carrier component comprising a diorganopolysiloxane fluid. This combination of materials can be used alone or in combination with the above-described silicone resin copolymer.

The organosiloxane resin adhesive is preferably used in the composition of the present invention such that the weight ratio of the resin to the diorganopolysiloxane fluid is from about 1:9 to about 10:1, more preferably from about 1:1 to about 5:1, even more preferably from about 1:1 to about 3:1, and wherein the total concentration of the organosiloxane resin and the diorganopolysiloxane fluid ranges from about 1% to about 40%, more preferably from about 1% to about 30%, even more preferably from about 1% to about 20%, by weight of the composition.

The organosiloxane resin adhesive for use in the compositions of the present invention include combinations of  $R_3SiO_{1/2}$  (M units),  $R_2SiO$  (D units),  $RSiO_{3/2}$  (T units),  $SiO_2$  (Q units) units in ratios to each other that satisfy the relationship  $R_nSiO_{(4-n)/2}$  where n is a value between 1.0 and 1.50 and R is a methyl group. Note that a small amount, up to 5%, of silanol or alkoxy functionality may also be present in the resin structure as a result of processing. The organosiloxane resins are solids at about 25°C and have a molecular weight range of from about 1,000 to about 10,000 grams/mole.



and is preferably forms a solution with the organosiloxane resin and any other liquid carrier materials in the composition.

The diorganosiloxane fluid for use herein comprises repeating units that correspond to the formula  $(R_2SiO)$ , where R is a monovalent hydrocarbon radical containing from 1 to 6 carbon atoms, preferably R is selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-butyl, amyl, hexyl, vinyl, allyl, cyclohexyl, phenyl, fluoroalkyl and mixtures thereof. The organopolysiloxane fluid may contain one or more of these hydrocarbon radicals as substituents on the siloxane polymer backbone. The organopolysiloxane fluid may be terminated by triorganosilyl groups of the formula  $(R'_3Si)$  where R' is a radical selected from monovalent hydrocarbons containing from 1-6 carbon atoms, hydroxyl groups, alkoxy groups and mixtures thereof.

Non limiting examples of preferred organopolysiloxane fluids for use herein include poly(dimethylsiloxane) [PDMS] materials such as those available from General Electric as SE30, SE72, SE84, Viscasil @100M, Viscasil @300M, and Baysilone Fluid M 500,000.

#### Optional Ingredients

The personal cleansing compositions of the present invention may further comprise other optional ingredients that may modify the physical, chemical, cosmetic or aesthetic characteristics of the compositions or serve as additional "active" components when deposited on the skin. The compositions may also further comprise optional inert ingredients. Many such optional ingredients are known for use in personal care compositions, and may also be used in the personal cleansing compositions herein, provided that such optional materials are compatible with the essential materials described herein, or do not otherwise unduly impair product performance.

Such optional ingredients are most typically those materials approved for use in cosmetics and that are described in reference books such as the CTFA Cosmetic Ingredient Handbook, Second Edition, The Cosmetic, Toiletries, and Fragrance Association, Inc. 1988, 1992. Non limiting examples of such optional ingredients include preservatives, deodorants, fragrances, deodorant perfumes, coloring agents or dyes, thickeners, sensates, sunscreens, gallants or other suspending agents, pH modifiers, co-solvents or other additional solvents, emollients, pharmaceutical actives, vitamins, and combinations thereof.

Other optional ingredients include silicone elastomer powders and fluids to provide any of a variety of product benefits, including improved product stability, application cosmetics,

### **Method of Manufacture**

The topical compositions of the present invention may be prepared by any known or otherwise effective technique, suitable for making and formulating the desired product form. Specific non-limiting examples of such methods as they are applied to specific embodiments of the present invention are described in the following examples.

### **EXAMPLES**

The following examples further describe and demonstrate embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention. All exemplified amounts are concentrations by weight of the total composition, i.e., wt/wt percentages, unless otherwise specified.

The personal cleansing compositions described below provide deposition and adherence of the film-forming material onto the hair, skin or nails. When applied to the hair, the compositions provide hair styling and conditioning benefits, including hair volume reduction. When applied to the skin, or the skin and hair, the compositions help to prevent or inhibit skin irritation that would otherwise be associated with composition in the absence of the film-forming polymer component. Each of the exemplified compositions, therefore, provides improved film-forming benefits on the surfaces on which each is applied.

### **Personal Cleansing Compositions**

The following examples described below are non-limiting examples of personal cleansing compositions of the present invention. These compositions can be applied to the hair, nail or skins as a rinse-off cleansing product.

The cleansing compositions of the present invention, including the exemplified shampoo embodiments described below, may be prepared using conventional formulation and mixing techniques. For example, the PSA is first to be dissolved in the C10-11 isoparaffin, and the PSA/ C10-11 isoparaffin combination is then added to a premix of the surfactants, or some portion of the surfactants, and the solid components which had been heated to melt the solid components e.g., about 87°C. This mixture is then pumped through a high shear mill and cooled, and then the remaining components are mixed in. Alternatively, the PSA/ C10-11 isoparaffin premix can be added to this final mix, after cooling. The composition has a final viscosity from

- (2) Available under the tradename PSA 7-4600 PSA Solids from Dow Corning Co. (USA)  
 (3) Available under the tradename PSA 7-4500 PSA Solids from Dow Corning Co. (USA)  
 (4) Available under the tradename Varisoft CB110 from Witco Chemical Co. (Dublin, Ohio, USA)

Table 2: Body Wash Compositions

Ingredient	Ex. 2.1	Ex. 2.2	Ex. 2.3	Ex. 2.4	Ex. 2.5	Ex. 2.6	Ex. 2.7	Ex. 2.8	Ex. 2.9	Ex. 10
Ammonium Laureth Sulfate	---	---	---	---	---	---	---	---	---	---
Ammonium Lauryl Sulfate	---	---	---	---	---	---	---	---	---	---
Sodium Lauroamphoacetate	---	---	---	---	---	---	---	---	---	---
Sodium Laureth Sulfate	7.54	7.54	7.54	7.54	7.54	7.54	7.54	7.54	7.54	7.54
Cocamidopropyl Betaine	6.67	6.67	6.67	6.67	6.67	6.67	6.67	6.67	6.67	6.67
Sodium Lauroyl Sarcosinate	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65
Citric Acid	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26	0.26
Trihydroxystearin	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Starch Copolymer	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Guar										
Hydroxypropyltrimonium Chloride	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Lauryl Alcohol	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65
PSA 7-4100/Trimethylated silica treated with dimethyl siloxane (70% in isododecane) (1)	7.14	28.57	14.29	---	---	---	---	---	---	---
PSA 7-4100/Trimethylated silica treated with dimethyl siloxane (40% in isododecane) (1)	---	---	---	25.00	---	---	---	---	---	---
PSA 7-4100/Trimethylated silica treated with dimethyl siloxane (50% in isopropyl myristate) (1)	---	---	---	---	20	---	---	---	---	---

- (4) Available under the tradename PSA 7-4400 Solids from Dow corning Co. (USA)  
 (5) Available under the tradename PSA 7-4500 Solids from Dow corning Co. (USA)  
 (6) Available under the tradename PSA 7-4600 Solids from Dow corning Co. (USA)  
 (7) Available under the tradename MQ SR1000 Resin from GE Silicones (USA)  
 (8) Available under the tradename SE30 Silicone Gum from GE Silicones (USA)

Table 3: Body Wash Compositions

Ingredient	Ex. 3.1	Ex. 3.2	Ex. 3.3
Ammonium Laureth Sulfate	3.00	---	---
Ammonium Lauryl Sulfate	4.00	---	---
Sodium Lauroamphoacetate	4.00	---	---
Sodium Laureth Sulfate	---	7.54	7.54
Cocamidopropyl Betaine	---	6.67	6.67
Sodium Lauroyl Sarcosinate	4.50	0.65	0.65
Citric Acid	0.26	0.26	0.26
Trihydroxystearin	1.00	1.00	1.00
Starch Copolymer	0.50	0.50	0.50
Guar			
Hydroxypropyltrimonium Chloride	0.50	0.50	0.50
Lauryl Alcohol	0.65	0.65	0.65
PSA 7-4100/Trimethylated silica treated with dimethyl siloxane (70% in isododecane) (1)	14.2 9	28.5 7	14.29
PSA 7-4100/Trimethylated silica treated with dimethyl siloxane (40% in isododecane) (1)	---	---	---

Water	qs	qs	qs
	100	100	100

- (1) Available under the tradename PSA 7-4100 Solids from Dow corning Co. (USA)
- (2) Available under the tradename PSA 7-4200 Solids from Dow corning Co. (USA)
- (3) Available under the tradename PSA 7-4300 Solids from Dow corning Co. (USA)
- (4) Available under the tradename PSA 7-4400 Solids from Dow corning Co. (USA)
- (5) Available under the tradename PSA 7-4500 Solids from Dow corning Co. (USA)
- (6) Available under the tradename PSA 7-4600 Solids from Dow corning Co. (USA)
- (7) Available under the tradename MQ SR1000 Resin from GE Silicones (USA)
- (8) Available under the tradename SE30 Silicone Gum from GE Silicones (USA)

(A) from 0.1% to 30% by weight of a film-forming material comprising an organosiloxane resin and a diorganosiloxane fluid at a weight ratio of said resin to said fluid of from 1:9 to 10:1.

(B) from 0.5% to 30% by weight of a cleansing surfactant; and

(C) from 20% to 99% by weight of a carrier liquid;

wherein the personal cleansing composition is a rinse-off composition for application to the hair or skin.

8. The personal cleansing composition of Claim 7, further characterized wherein the weight ratio of the organosiloxane resin to the diorganosiloxane fluid is from 1:1 to 3:1

9. The personal cleansing composition of Claim 7, further characterized wherein the diorganosiloxane fluid has a viscosity of from 100 to 1,000,000 cs at 25°C and the organic substituents on the diorganopolysiloxane fluid are selected from the group consisting of methyl, ethyl, and vinyl radicals.

10. The personal cleansing composition of Claim 7, further characterized wherein the organosiloxane resin is a condensation product of  $\text{SiO}_2$  and  $\text{R}_3(\text{SiO})_{0.5}$  units; wherein each R group is independently selected from the group consisting of methyl, ethyl, propyl and vinyl radicals; and the molar ratio of  $\text{SiO}_2$  units to  $\text{R}_3(\text{SiO})_{0.5}$  units in the silicone resin is from 0.6 to 1.0.

11. The personal cleansing composition of Claim 7, further characterized wherein the organosiloxane resin represents from 1% to 10% by weight of the composition, and the diorganosiloxane fluid represents from 1% to 10% by weight of the composition.

12. The personal cleansing composition of Claim 7, further characterized wherein the carrier liquid is an aqueous liquid and the composition comprises from 20% to 98% by weight of water, preferably 30 % to 98% by weight of water.

13. The personal cleansing composition of Claim 7, further characterized wherein the composition further comprises from 0.1% to 20% by weight of solid particulates.

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 02/30096

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K7/06 A61K7/48		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPQ-Internal, PAJ, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 246 694 A (BIRTHWISTLE DAVID H) 21 September 1993 (1993-09-21) column 1, line 5-10 column 2, line 64 -column 4, line 47 -----	1-6,14
<input type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "Z" document member of the same patent family		
Date of the actual completion of the international search  3 December 2002		Date of mailing of the international search report  12 12 02
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2200 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3018		Authorized officer  Simon, F

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-6,14

Personal cleansing compositions comprising:

(a1) 0.1-30 wt-% of a silicone resin copolymer as a condensation product of a diorganosiloxane fluid and an organosiloxane resin,

(b) 0.5-30 wt-% of a cleansing surfactant and

(c) 20-98.9 wt-% of a liquid carrier;

and corresponding method of cleansing the skin.

2. Claims: 7-13,15

Personal cleansing compositions comprising:

(a2) 0.1-30 wt-% of a film forming material comprising a mixture of an organosiloxane resin and a diorganosiloxane fluid at a weight ratio of said resin to said fluid of from 1:9 to 10:1,

(b) 0.5-30 wt-% of a cleansing surfactant and

(c) 20-99 wt-% of a liquid carrier;

and corresponding method of cleansing the skin.





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<b>(21) International Application Number:</b> PCT/US91/07771 <b>(22) International Filing Date:</b> 21 October 1991 (21.10.91) <b>(30) Priority data:</b> 606,289 31 October 1990 (31.10.90) US <b>(71) Applicant:</b> THE PROCTER & GAMBLE COMPANY [US/US]; One Procter & Gamble Plaza, Cincinnati, OH 45202 (US). <b>(72) Inventors:</b> WONG, Teresa, Kinhuen ; 7488 Fitzroy Ct., Cincinnati, OH 45241 (US). WARREN, Raphael ; 6258 Robinson Road, Cincinnati, OH 45213 (US). <b>(74) Agent:</b> REED, T., David; The Procter & Gamble Com- pany, Ivorydale Technical Ctr., 5299 Spring Grove Ave., Cincinnati, OH 45217-1087 (US).		<b>(81) Designated States:</b> AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (Eu- ropean patent), GN (OAPI patent), GR (European pa- tent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC, MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European pa- tent), NO, PL, RO, SD, SE, SE (European patent), SN (OAPI patent), SU*, TD (OAPI patent), TG (OAPI pa- tent).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the</i> <i>claims and to be republished in the event of the receipt of</i> <i>amendments.</i>
<b>(54) Title:</b> HAIR GROWTH REGULATING COMPOSITION COMPRISING EPITHELIUM CELL SUPERNATANT-DE- RIVED GROWTH FACTOR  <b>(57) Abstract</b>  The present invention relates to a composition for regulating hair growth comprising a safe and effective amount of super- natant derived from a culture of epithelial cells which comprises a growth stimulating factor with characteristics of mitogenicity to dermal papilla cells, mitogenicity to 3T3 cells, lack of mitogenicity to epidermal cells, and a molecular weight of greater than about 3000D; and a pharmaceutically-acceptable carrier.		

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HAIR GROWTH REGULATING COMPOSITION COMPRISING EPITHELIUM  
CELL SUPERNATANT-DERIVED GROWTH FACTOR

5

TECHNICAL FIELD

The present invention relates to novel compositions which regulate hair growth.

BACKGROUND OF THE INVENTION

10 Society in general continues to attach a stigma to hair loss. The desire for a healthy full head of hair has resulted in a variety of approaches to the "curing" of baldness. Investigation of the hair bulb has been among the multitude of hair growth studies that have been reported in the literature. There are two  
15 essential features of the hair follicle. These include the epithelia and a specialized dermal compartment called the dermal papilla. The epithelia give rise to the epidermal stem cells which in turn give rise to the outer root sheath, giving rise to the matrix cell, which gives rise to the inner root sheath and  
20 hair fiber. The size of the dermal papilla is related to the size of the hair follicle, and the size of the follicle is related to the size of the hair produced. For example, terminal hair follicles on the scalp of haired individuals are longer and produce long, thick hair. These follicles contain large dermal  
25 papilla. In contrast, vellus follicles commonly observed on a bald scalp are small and produce short, thin hair. These vellus follicles contain a small dermal papilla. Similar observations relating to the relationship between the size of the papilla and the hair follicle, and ultimately hair growth, have been made in  
30 animals having fur. The specific factors which regulate the size of the dermal papilla may ultimately regulate hair growth.

European Patent Application No. 0,215,274, Eisinger, assigned to the Memorial Hospital for Cancer and Allied Diseases, published March 25, 1987, discloses the sonification of epidermal  
35 cells to extract the intracellular materials. Methods to enhance wound healing, regenerate epidermis, and enhance hair growth via application of the epidermal cell extract are also disclosed.

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stimulating factor with characteristics of mitogenicity to dermal papilla cells, mitogenicity to 3T3 cells, lack of mitogenicity to epidermal cells, and a molecular weight of greater than about 3,000 daltons; and a pharmaceutically-acceptable carrier.

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DETAILED DESCRIPTION OF THE INVENTION

As used herein, "mitogenicity" means an ability to stimulate growth (mitosis) in cells.

As used herein, "regulating hair growth" means inducing the formation of a greater number of hair strands, and/or increasing the diameter of the hair strand, and/or lengthening the hair strand, and/or preventing, retarding, or arresting the process of hair loss.

As used herein, "proliferating cells" means cells undergoing mitosis.

As used herein, "epithelial cells" refers to the cells which cover all the free surfaces, cutaneous, mucous, and serous, including the glands and other structures derived therefrom, e.g., corneal, esophageal, epidermal, and hair follicle epithelial cells, but not including amnion epithelial cells. Such cells may be normal non-malignant cells, or transformed/immortalized cells.

As used herein, "hair follicle epithelial cells" refers to epithelial cells which surround the dermal papilla in the hair follicle, e.g., stem cells, outer root sheath cells, matrix cells, and inner root sheath cells. Such cells may be normal non-malignant cells, or transformed/immortalized cells.

As used herein, "epidermal cells" refers to epithelial cells in the epidermis. Such cells may be normal non-malignant cells, or transformed/immortalized cells.

As used herein, "epidermis" refers to the continuous stratified keratinizing cell layer encompassing the entire organism and terminating at bodily orifices in mucocutaneous junctions, but not including the hair follicle epithelial cells.

As used herein, "topical application" means directly laying on or spreading on outer skin.

As used herein, "transformed cells" refers to cells which have spontaneously converted to a state of unrestrained growth, i.e., they have acquired the ability to grow through an

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derived from the hair growth factor can also show activity in regulating hair growth.

According to a preferred embodiment of the invention, the cell free epithelial cell culture supernatant is concentrated at  
5 least 40 to 50 times, preferably at least 100 times, to provide a concentrate containing the hair growth factor, having a protein level not greater than 10 mg/ml, preferably 2 to 3 mg/ml.

The amount of the hair growth factor to be incorporated with a suitable vehicle into compositions for topical use can vary  
10 widely, but in general, an amount expressed as protein of from about 0.00001% to about 20%, preferably from about 0.001% to about 10%, more preferably from about 0.01% to about 5% by weight of the composition will provide an adequate dose of hair growth factor to the skin following topical application.

15 The amount of the hair growth factor to be incorporated with a suitable vehicle into compositions for cutaneous injection can vary widely, but in general, an amount expressed as a protein of from about 0.00001% to about 10%, preferably from about 0.001% to about 10%, more preferably from about 0.01% to about 10%, by  
20 weight of the composition will provide an adequate dose of hair growth factor to the target area following cutaneous injection.

The following examples are intended to illustrate the process for obtaining the growth stimulating factor as applied to a particular sample. It is not intended to limit the invention.

#### 25 EXAMPLE I

##### Preparation of Epidermal Cell Derived Growth Stimulating Factor

Human foreskin epidermal cells are prepared according to the method of S. T. Boyce and R. G. Ham (J Tissue Culture Meth 9, 83-93, 1985) with the following modifications. After treatment  
30 of foreskin with collagenase, the epidermis is placed in 0.0125% trypsin in Hepes buffered saline. The epidermis is then triturated to release individual epidermal cells. The epidermal cells are grown in a cell culture medium of KGM (Clonetics; #3001). Epidermal cells are subcultured using 3.0 Units/ml  
35 dispase at 37°C until the cells detach from the surface. KGM is then added at a volume ratio of 5:1 to dispase. The cell suspension is then transferred into a conical tube and centrifuged at

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follicles are sequentially treated with trypsin again. The cell suspension is collected and centrifuged at 200 X G for 10 minutes. The cells are rinsed once again in DMEM without serum. The epithelial cells are grown in a cell culture medium of KGM (Clonetics; #3001). Epithelial cells are subcultured using 3.0 Units/ml dispase at 37°C until the cells detach from the surface. KGM is then added at a volume ratio of 5:1 to dispase. The cell suspension is then transferred into a conical tube and centrifuged at 200 X G for 5 min. The cells are resuspended with fresh KGM for plating. The cells are grown to passage #2 at which time cells are rinsed and the culture medium changed to 'Defined Medium' (medium which does not contain pituitary extract nor the following growth factors normally present in the culture medium, including hydrocortisone, insulin, and epidermal growth factor; KBM Clonetics #3101). The epithelial cells are incubated in this medium for up to 48 hours at which time the culture medium is decanted. This medium ('Conditioned Defined Medium') is then centrifuged at 100000 x G for one hour. The medium is fractionated and concentrated by ultrafiltration using an Amicon Centricon-3 filter having a molecular weight cutoff of 3000D. The retentate having a molecular weight greater than 3000 will contain all the growth factor activity as determined in the dermal papilla cell mitogen assay below, whereas there will be no activity in the filtrate which contains material having a molecular weight less than 3000D.

Alternative methods for fractionating and concentrating the conditioned medium can include dialyzing the medium against a membrane having a specific molecular weight cutoff, followed by lyophilizing the medium, and finally reconstituting the medium into a suitable buffer.

### EXAMPLE III

#### Dermal Papilla Cell Mitogen Assay

##### A. Preparation of Human Scalp Dermal Papilla Cells

The human scalp dermal papilla (hDP) cells are prepared using a modified procedure of existing methodologies (A. G. Messenger, Br J Dermatol 110, 685-689, 1984; and C. A. B. Jahoda and R. F. Oliver, Br J Dermatol 105, 623-627, 1981; and C. A. B.

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and antibiotics ('Complete DMEM'). The following day the medium is changed to Complete DMEM. The following day the medium is changed to DMEM containing 0.5% fetal calf serum. During the last four hours of a 24 hour incubation, the cells are incubated with [methyl-3-H]-thymidine. This time point represents the baseline mitotic activity of the dermal papilla cells. The radiolabelled cells are then solubilized in a solution containing 0.1% sodium dodecyl sulfate, 0.05mM EDTA, and 1.0mM Tris pH 8.0. Trichloroacetic acid and ethanol precipitable radiolabelled DNA is determined and normalized to the total content of cellular DNA in the sample (C. Lebarca and K. Paigen, *Analyt Biochem* 102, 344-351, 1980).

The remaining dermal papilla cells are then exposed to (a) fresh Complete DMEM (positive control) (b) fresh DMEM containing 0.5% fetal calf serum (negative control), (c) 1:1 mixture of fresh DMEM containing 0.5% fetal calf serum and Conditioned Defined Medium, or (d) 1:1 mixture of fresh DMEM containing 0.5% fetal calf serum and Conditioned Sham Medium. The media used in (c) and (d) is adjusted to a final fetal calf serum concentration of 0.5% and 1.0 mM CaCl<sub>2</sub> before adding to the hDP cells. During the last four hours of a 24 hour incubation, the cells are incubated with [methyl-3-H]-thymidine. The cells are processed for acid and ethanol precipitable radiolabelled DNA as described above for the baseline measurement.

The results show that the Conditioned Defined Medium induces a significant increase in thymidine incorporation relative to the sham control.

#### EXAMPLE IV

##### 3T3 Cell Mitogen Assay

The 3T3 cell mitogen assay is based on the assay described by Scher, C. D., et al. *Nature* 281, 390-392, 1979; Cohen, S. and Carpenter, G. *Proc Nat Acad Sci, USA* 72, 1317-1320, 1975; and Gospodarowicz, D *F Biol Chem* 250, *D J Biol Chem* 250, 2515-2520, 1975.

Balb/c 3T3 cells are plated and grown in a 24-well tissue culture dish in Dulbecco's Modified Eagle's Medium (DMEM) + 10% newborn calf serum. The medium is changed three times a week

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- cells are rinsed and solubilized in a solution containing 0.1% sodium dodecyl sulfate, 0.05mM EDTA, and 1.0 mM Tris pH 8.0. Trichloroacetic acid and ethanol/ether precipitable radiolabelled DNA is determined and normalized to the total content of cellular DNA in the sample. For the remaining cells, after the five day incubation, the medium ('old medium') is removed and saved. To one set of three wells old medium is added back ('negative control'). To a second set of wells, fresh KGM is added ('positive control'). To a third set of wells, a 1:1 mixture of old medium and conditioned defined medium is added ('test'). To a fourth set of wells a 1:1 mixture of old medium and sham conditioned medium is added ('sham control'). During the last four hours of a 24 hour incubation, the cells are incubated and radiolabelled with thymidine as described above.
- 15        The resulting data will show that Conditioned Defined Medium does not contain factors which are mitogenic to human epithelial cells relative to the sham control.

## EXAMPLE VI

Sensitivity to Proteases20    A.    Protease Sensitivity: Trypsin

- Conditioned medium derived from foreskin epidermal cells is prepared as described previously. The medium is treated with trypsin type III (Sigma T-8253) at a final concentration of up to 100 ug/ml at 37°C for up to four hours. Soybean trypsin inhibitor type I-S (Sigma Y-9003) is then added to a final concentration of 1 mg/ml. The mixture is then centrifuged at 20000 G for thirty minutes, decanted, and filter sterilized. This medium is tested in the dermal papilla cell mitogen assay. The data show that the mitogenic activity of the conditioned medium is not affected by trypsin treatment relative to a control that is treated identically except without trypsin.

B.    Protease Sensitivity: Chymotrypsin

- Conditioned medium derived from foreskin epidermal cells is prepared as described previously. The medium is treated with chymotrypsin type I-S (Sigma C-7762) at a final concentration of up to 100 ug/ml at 37°C for up to five hours. Soybean trypsin inhibitor type I-S (Sigma Y-9003) is then added to a final

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desired target at an appropriate concentration. As used herein, "pharmaceutically acceptable carrier" means a filler/diluent substance which is suitable for administration to a human or lower animal. The carrier can itself be inert or it can possess physiological or pharmaceutical benefits of its own. The nature of the carrier will be dictated by the method chosen for administration of the composition. The method of administration of the growth stimulating factor composition may range from internal methods such as injection to external topical methods.

10 A preferred method of administration of the growth stimulating factors is by cutaneous injection. The carrier for facilitation of such administration would preferably comprise water or a saline solution.

15 A more preferred method of administration of the growth stimulating factors is by topical application. Topical application is preferably achieved with compositions in the forms of sprays, tonics, creams, lotions, shampoos, and the like.

20 Topical compositions of the present invention can be formulated as liquids, for example as a lotion, cream, shampoo, conditioner or milk. Such liquid compositions may be formulated for use in conjunction with an applicator such as a roll-ball applicator, or a spray device such as an aerosol can containing propellant, or a container fitted with a pump to dispense the liquid product.

25 Alternatively, the compositions of the invention can be solid or semi-solid, for example sticks, creams or gels. Such solid or semi-solid compositions may be formulated for use in conjunction with a suitable applicator or simply a tube, or bottle, or as a liquid-impregnated fabric, such as a tissue wipe.

30 The selection of a carrier for this purpose presents a wide range of possibilities depending on the required product form of the composition. Suitable vehicles can be classified as described hereinafter.

35 The term "topical carrier" refers to substances which can act as diluents, dispersants, or solvents for the growth stimulating factors which therefore ensure that it can be applied to and distributed evenly over the selected target at an appropriate



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d. Acetoglyceride esters, such as acetylated monoglycerides.

e. Ethoxylated glycerides, such as ethoxylated glyceryl monostearate.

5 f. Alkyl esters of fatty acids having 10 to 20 carbon atoms. Methyl, isopropyl and butyl esters of fatty acids are useful herein. Examples include hexyl laurate, isohexyl laurate, isohexyl palmitate, isopropyl palmitate, isopropyl myristate, decyl oleate, isodecyl oleate, hexadecyl stearate, decyl  
10 stearate, isopropyl isostearate, diisopropyl adipate, diisohexyl adipate, dihexyldecyl adipate, diisopropyl sebacate, lauryl lactate, myristyl lactate, and cetyl lactate.

g. Alkenyl esters of fatty acids having 10 to 20 carbon atoms. Examples thereof include oleyl myristate, oleyl stearate,  
15 and oleyl oleate.

h. Fatty acids having 8 to 22 carbon atoms. Suitable examples include pelargonic, lauric, myristic, palmitic, stearic, isostearic, hydroxystearic, oleic, linoleic, ricinoleic, arachidonic, behenic, and erucic acids.

20 i. Fatty alcohols having 8 to 22 carbon atoms. Lauryl, myristyl, cetyl, hexadecyl, stearyl, isostearyl, hydroxystearyl, oleyl, ricinoleyl, behenyl, erucyl, and 2-octyl dodecyl alcohols are examples of satisfactory fatty alcohols.

j. Fatty alcohol ethers. Ethoxylated fatty alcohols of 8  
25 to 20 carbon atoms include the lauryl, cetyl, stearyl, isostearyl, oleyl, and cholesterol alcohols having attached thereto from 1 to 50 ethylene oxide groups or 1 to 50 propylene oxide groups, or a mixture thereof.

k. Ether-esters such as fatty acid esters of ethoxylated  
30 fatty alcohols.

l. Lanolin and derivatives. Lanolin, lanolin oil, lanolin wax, lanolin alcohols, lanolin fatty acids, isopropyl lanolate, ethoxylated lanolin, ethoxylated lanolin alcohols, ethoxylated cholesterol, propoxylated lanolin alcohols, acetylated lanolin,  
35 acetylated lanolin alcohols, lanolin alcohols linoleate, lanolin alcohols ricinoleate, acetate of lanolin alcohols ricinoleate, acetate of ethoxylated alcohols-esters, hydrogenolysis of

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s. Sterols. Cholesterol, cholesterol fatty acid esters are examples thereof.

t. Amides such as fatty acid amides, ethoxylated fatty acid amides, solid fatty acid alkanolamides.

5       The lotions further preferably comprise from 1% to 10%, more preferably from 2% to 5%, of an emulsifier. The emulsifiers can be nonionic, anionic or cationic. Examples of satisfactory nonionic emulsifiers include fatty alcohols having 10 to 20 carbon atoms, fatty alcohols having 10 to 20 carbon atoms condensed with 2 to 20 moles of ethylene oxide or propylene oxide, alkyl phenols with 6 to 12 carbon atoms in the alkyl chain condensed with 2 to 20 moles of ethylene oxide, mono- and di-fatty acid esters of ethylene oxide, mono- and di-fatty acid esters of ethylene glycol wherein the fatty acid moiety contains from 10 to 20 carbon atoms, diethylene glycol, polyethylene glycols of molecular weight 200 to 6000, propylene glycols of molecular weight 200 to 3000, glycerol, sorbitol, sorbitan, polyoxyethylene sorbitol, polyoxyethylene sorbitan and hydrophilic wax esters. Suitable anionic emulsifiers include the fatty acid soaps, e.g. sodium, potassium and triethanolamine soaps, wherein the fatty acid moiety contains from 10 to 20 carbon atoms. Other suitable anionic emulsifiers include the alkali metal, ammonium or substituted ammonium alkyl sulfates, alkyl arylsulfonates, an alkyl ethoxy ether sulfonates having 10 to 30 carbon atoms in the alkyl moiety. The alkyl ethoxy ether sulfonates contain from 1 to 50 ethylene oxide units. Satisfactory cationic emulsifiers are the quaternary ammonium, morpholinium and pyridinium compounds. Certain of the emollients described in preceding paragraphs also have emulsifying properties. When a lotion is formulated containing such an emollient, an additional emulsifier is not needed, though it can be included in the composition.

35       The balance of the lotion is water or a C<sub>2</sub> or C<sub>3</sub> alcohol, or a mixture of water and the alcohol. The lotions are formulated by simply admixing all of the components together. Preferably the compound of the present invention is dissolved in the mixture. Conventional optional components can be included. One such additive is a thickening agent at a level from 1% to 10% of

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#### 4. Gels

Gel compositions can be formulated by simply admixing a suitable thickening agent to the previously described solution compositions. Examples of suitable thickening agents have been previously described with respect to the lotions.

The gel compositions comprise an effective amount (preferably from about 0.01% to about 10%, more preferably from about 1% to about 5%) of the growth stimulating factors; from 5% to 75%, preferably from 10% to 50%, of an organic solvent as previously described; from 0.5% to 20%, preferably from 1% to 10% of the thickening agent; the balance being water.

#### 5. Solids

Compositions of solid forms have use as stick-type compositions intended for application to the scalp or other parts of the body. Such compositions comprise an effective amount (preferably from about 0.01% to about 10%, more preferably from about 1% to about 5%) of the growth stimulating factors, and from 50% to 98%, preferably from 60% to 90%, of the previously described emollients. This composition can further comprise from 1% to 20%, preferably from 5% to 15%, of a suitable thickening agent, and optionally emulsifiers and water. Thickening agents previously described with respect to lotions are suitable herein.

#### Penetration Enhancers

The presence of a penetration enhancer can potentiate the benefit of the hair growth stimulating factor by improving its delivery through the stratum corneum to its site of action in the immediate environment of the hair follicle proximate to the dermal papilla.

The penetration enhancer can accordingly function in a variety of ways. It can, for example, improve the distribution of the hair growth promoter on the skin surface. Alternatively, it can increase its partition into the skin from the composition when applied topically, so aiding its passage to its site of action. Other mechanisms enhancing the benefit of the growth stimulating factors may also be involved.

Examples of penetration enhancers include, but are not limited to: 1-dodecylazacycloheptan-2-one in combination with

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European Patent Application 043 738, Wickett, Cooper and Loomans, published January 13, 1982); a carrier comprising a C<sub>6</sub>-C<sub>14</sub> primary alkanol and a propane or butane diol (See European Patent Application 013 459, Wickett, Cooper and Loomans, published July 23, 1980);

#### Other Hair Growth Stimulants

The composition according to the invention can also optionally comprise other hair growth stimulants capable of functioning in different ways to enhance the benefit of the growth stimulating factors. Examples of other substances which themselves possess the ability to regulate hair growth include, but are not limited to, minoxidil, retinoic acid, diazoxide, gly-his-lys (also known as liver cell growth factor) and its transition metal derivatives, cyclosporine, anti-inflammatories, calcium channel blockers, anti-bacterials, nonionic surfactants, mucopolysaccharides, antiandrogens, glycosidase inhibitors, and glycosaminoglycanase inhibitors.

#### Protein Stabilizing Agents

The hair growth factor is proteinaceous, and therefore its benefit in promoting hair growth can be maintained or improved by including a protein stabilizing agent in the composition according to the invention. As an example of this effect, it is to be noted that the skin contains natural proteases which might at least partially degrade the hair growth promoter. Therefore, the presence of a protein stabilizing agent such as a protease inhibitor or a secondary protein which will compete with the hair growth promoter for degradation by the natural skin proteases, can protect the hair growth promoter until it reaches the immediate environment of the hair bulb.

Examples of a protein stabilizing agent accordingly include glycerol, ethylenediaminetetraacetic acid, cysteine,  $\alpha_2$ -macroglobulin, serum, and other proteinase inhibitors.

#### Other Ingredients

The composition according to the invention can contain ingredients other than those already mentioned, depending on the form of the intended product. It is, for example, possible to

A more preferred method of applying the compositions according to the present invention involves topical application to the scalp of a human subject to regulate hair growth, particularly where the head is already bald, or where there is evidence to suggest a person will go bald (i.e., hair loss). The amount of the composition and the frequency of application to the hair and/or scalp can vary widely, depending on personal needs, but it is suggested as an example that topical application range from about 1 to about 10 times daily, preferably from about 2 to about 6 times daily, more preferably from about 3 to about 4 times daily, and most preferably once per day. The composition for topical application will contain from about 1 ng/cm<sup>2</sup> to about 1 mg/cm<sup>2</sup> of the growth stimulating factor per dose, preferably from about 100 ng/cm<sup>2</sup> to about 0.9 mg/cm<sup>2</sup>, more preferably from about 0.5 µg/cm<sup>2</sup> to about 0.7 mg/cm<sup>2</sup>, and most preferably from about 10 µg/cm<sup>2</sup> to about 0.5 mg/cm<sup>2</sup>. The period of topical application would preferably be over a period of from about one month to about ten years, more preferably from about three months to about two years, more preferably still from about six months to about one year, thereby resulting in regulation of hair growth.

The following examples further describe and demonstrate the preferred embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration, and are not to be construed as limitations of the present invention since many variations thereof are possible without departing from its spirit and scope.

Examples VIII-X illustrate a tonic according to the invention which is suitable for topical application to the scalp in order to promote hair growth. The lotion has the following formulation:

	<u>Example VIII</u>	<u>Example IX</u>	<u>Example X</u>
	(%w/w)	(%w/w)	(%w/w)
Hair growth factor	0.1	1.0	10.0
Ethanol	10.0	15.0	15.0
35 Glycerol	1.0	2.0	3.0
Perfume	0.2	0.2	0.2
Water	qs	qs	qs

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The emulsion was prepared by taking 10 parts by volume of the oily phase and to it adding slowly with stirring 90 parts by volume of the aqueous phase.

Example XV illustrates an oil-in-water cream containing a hair growth factor according to the invention.

Example XV

(%w/w)

Oil Phase

	Cetearyl alcohol	5.0
10	Silicone oil, 200 fluid	1.0
	Isopropyl myristate	2.0
	Sodium stearoyl-2-lactylate	2.0

Aqueous Phase

	Propylene glycol	5.0
15	Sodium citrate	0.2
	Hair growth factor	0.1
	Perfume	0.1
	Purified water	qs to 100

The cream was prepared by mixing the oil phase and heating to 65°C. Combine the aqueous phase and heat to 70°C. Add the aqueous phase to the oil phase with suitable agitation. Mix with moderate agitation while cooling.

The following examples XVI-XVIII illustrate shampoos for use in washing the hair and scalp, and for regulating hair growth on the scalp.

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The shampoo is applied to the scalp at a dose of one ml. The shampoo is rubbed onto the scalp, and then rinsed off. The shampoo is reapplied to the scalp, rubbed onto the scalp and rinsed off.

- 5 Examples XIX-XXVII illustrate lotions according to the invention, each containing an activity enhancer which can be used topically in the treatment of bald or balding male or female heads, in order to regulate hair growth.

	<u>Example XIX</u>	<u>Example XX</u>	<u>Example XXI</u>
	(%w/w)	(%w/w)	(%w/w)
10 Minoxidil	0.5	2.0	5.0
Absolute ethanol	20.0	20.0	20.0
Propylene glycol	30.0	30.0	30.0
Hair growth factor	5.0	1.0	0.1
15 Perfume	0.2	0.2	0.2
Water	qs	qs	qs

	<u>Example XXII</u>	<u>Example XXIII</u>	<u>Example XXIV</u>
	(%w/w)	(%w/w)	(%w/w)
Cu II:Gly-his-lys-n-octyl ester	0.1	1.0	5.0
20 Absolute ethanol	20.0	20.0	20.0
Propylene Glycol	30.0	30.0	30.0
Hair growth factor	5.0	2.0	0.5
Perfume	0.2	0.2	0.2
Water	qs	qs	qs

	<u>Example XXV</u>	<u>Example XXVI</u>	<u>Example XXVII</u>
	(%w/w)	(%w/w)	(%w/w)
25 Furildioxime	0.1	1.0	5.0
Absolute ethanol	20.0	20.0	20.0
Propylene glycol	30.0	30.0	30.0
30 Hair growth factor	10.0	3.0	1.0
Perfume	0.2	0.2	0.2
Water	qs	qs	qs

- The following Examples XXVIII and XXIX illustrate injectable forms of the hair growth factor for promoting hair growth on the scalp.
- 35

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1. A composition for regulating hair growth characterized in that the composition comprises
  - 5 a. a safe and effective amount of a supernatant derived from a culture of epithelial cells which is characterized in that the supernatant comprises a growth stimulating factor, preferably the composition comprises from .01% to 10% of the growth stimulating factor, the factor having the following characteristics:
    - 10 i. mitogenicity to dermal papilla cells,
    - ii. mitogenicity to 3T3 cells,
    - iii. lack of mitogenicity to epidermal cells, and
    - iv. a molecular weight of greater than 3,000 daltons; and
  - 15 b. a pharmaceutically-acceptable carrier.
2. The composition of Claim 1 wherein the growth stimulating factor has the additional characteristic of decreased dermal papilla cell mitogen assay activity following treatment with chymotrypsin type I-S at a final concentration of up to 100 $\mu$ g/ml at 37°C for 5  
20 hours.
3. The composition according to any one of Claims 1 or 2 wherein the growth stimulating factor has the additional characteristic of retaining from 40% to 90% dermal papilla cell mitogen assay activity following heat treatment from 50° to 100°C.
- 25 4. The composition of any one of Claims 1-3 wherein the cells are hair follicle epithelial cells.
5. The composition of any one of Claims 1-3 wherein the cells are epidermal cells.  
5
6. The composition of any one of Claims 1-5 wherein the carrier is  
30 an injectable carrier.



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 91/07771

<b>I. CLASSIFICATION OF SUBJECT MATTER</b> (If several classification symbols apply, indicate all) <sup>6</sup>		
According to International Patent Classification (IPC) or to both National Classification and IPC Int.Cl.5                      C 07 K 15/00                      A 61 K 35/36                      A 61 K 7/06		
<b>II. FIELDS SEARCHED</b>		
Minimum Documentation Searched <sup>7</sup>		
Classification System	Classification Symbols	
Int.Cl.5	C 07 K                      A 61 K	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched <sup>8</sup>		
<b>III. DOCUMENTS CONSIDERED TO BE RELEVANT<sup>9</sup></b>		
Category <sup>10</sup>	Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>	Relevant to Claim No. <sup>13</sup>
X	EP,A,0215274 (MEMORIAL HOSPITAL FOR CANCER AND ALLIED DISEASES) 25 March 1987, see the whole document (cited in the application) ---	1
X	Proceedings of the National Academy of Sciences, USA, vol. 85, no. 6, March 1988, (US) Medical Sciences, M. Eisinger et al.: "Growth regulation of skin cells by epidermal cell-derived factors: Implications for wound healing", pages 1937-1941, see the whole article (cited in the application) ---	1
X	EP,A,0272920 (UNILEVER PLC) 29 June 1988, see the whole document ---	1,4,5,7 -9
A	WO,A,8907425 (GENETICS LTD) 24 August 1989, see page 41, lines 8-27; claims (cited in the application) ---                      -/-	1,4,5,7 -9
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><sup>10</sup> Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&amp;" document member of the same patent family</p> </div> </div>		
<b>IV. CERTIFICATION</b>		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
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International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	Mme N. KUIPER	

**ANNEX TO THE INTERNATIONAL SEARCH REPORT  
ON INTERNATIONAL PATENT APPLICATION NO.**

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This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 10/03/92  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A- 0215274	25-03-87	AU-B- 603993	06-12-90
		AU-A- 6113286	19-02-87
		JP-A- 62089622	24-04-87
EP-A- 0272920	29-06-88	AU-B- 605814	24-01-91
		AU-A- 8281287	23-06-88
		JP-A- 63185918	01-08-88
		US-A- 4832946	23-05-89
WO-A- 8907425	24-08-89	AU-A- 3218389	06-09-89
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EP-A- 0236014	09-09-87	AU-B- 598235	21-06-90
		AU-A- 6915187	27-08-87
		DE-A- 3771747	05-09-91
		JP-A- 62246508	27-10-87
		US-A- 4919664	24-04-90

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(54) **Cosmetic composition**

(57) This specification relates to a cosmetic composition containing art extract of *Croton birmanicus* as an effective ingredient, particularly, a hair-growing composition. The composition not only has excellent hair revitalizing actions such as an alopecia preventing effect and a hair generation accelerating effect, and a dandruff or itch inhibiting action, but also has a specific hair growth accelerating action through activation of hair dermal papilla cells or hair follicular epitheliocytes.

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## DESCRIPTION OF THE PREFERRED EMBODIMENT

[0013] The composition for the head in the invention includes compositions of any forms which can be used onto human heads, more specifically hairs and scalps. Such compositions can widely be used for hair revitalization, and in the present specification, "hair revitalization" is used in a conception to include acceleration of hair generation, prevention of alopecia, an action to inhibit dandruff or itch, etc., and further, an action to activate papillary cells or hair follicular epitheliocytes.

[0014] Although not limited by the theory, an extract from a plant belonging to the genus Croton of the family Euphorbiaceae as an effective ingredient used in the invention has a hair papilla activation action because it significantly proliferates human being-derived cultured hair dermal papilla cells, and, moreover, also has an action to lengthen the anagen of hair in the hair cycle because it maintains or accelerates proliferation of human being-derived cultured hair follicular epitheliocytes, as stated later.

[0015] Therefore, the extract has hair generation accelerating and alopecia preventing effects by acting directly on the structure (or constituents) itself of hair, and further also has a dandruff or itch inhibiting action because it shows its efficacy without having a bad influence on proliferation of the above cells.

[0016] Particularly, these effects and actions are surprising taking it into account that Croton oil obtained from germinal milk of seeds of Croton tiglium L., a plant belonging to the genus Croton of the family Euphorbiaceae (Tiglii Semen or croton seed) by pressing only has hair generating and hair growing actions significantly lower than the extract of the invention, and, on the other hand, has a skin stimulating action.

[0017] It is well-known that Croton oil contains 12-O-tetradecanoyl-phorbol 13-acetate (hereinafter, referred to as TPA) known as a tumor promoter which served as a basis of the establishment of the two-stage theory of a tumor promoter. This TPA is known to have a strong hair generating effect in C3H mice ("normal and Abnormal Epidermal Differentiation", edited by M. Seiji and I.A. Bernstein, pages 159-170, published in 1982 by Todai-Shuppan), but induces strong inflammation by topical application onto the ears of mice (P.L. Stanley et al., Skin Pharmacol. 1991; 4: 262-271) and brings about serious changes of epidermic cells (e.g., acanthosis, hyperkeratosis, etc.) by application onto the skin of Balb/c mice.

[0018] When such a background is taken into account, it is unexpected that the extract according to the invention shows significantly excellent hair generation accelerating effect and hair growing effect, and, moreover, hardly shows skin stimulating properties, and thus the usefulness of the screening or evaluation test method is proved which was established by the present inventors and uses cultured hair dermal papilla cells and cultured hair follicular epitheliocytes.

[0019] The extract used in the invention has its characteristic in the point that it is not a pressed oil from the germinal milk of seeds of the genus Croton of the family Euphorbiaceae, but obtained by extraction treatment.

[0020] Plants from which the extract of the invention can be obtained may be ones belonging to any species so long as they are plants being classified as the genus Croton and plants from which an extract meeting the object of the invention can be obtained. However, as preferred ones, there can be mentioned Croton birmanicus Muell. Arg. The plant is distributed chiefly in South-east Asia, and called HADSAKHYYN in Thailand.

[0021] The extract used in the invention can be obtained by immersing in an extracting solvent or refluxing with heating together with an extracting solvent leaves, stems including subterranean stems, roots, fruits, bark, etc. of the plant or the whole plant, subjecting the resultant mixture to filtration, and concentrating the filtrate. The extracting solvent can be any one so long as it is a solvent usually used for extraction, and, particularly, there can be mentioned one or a mixture of two or more selected from water-miscible organic solvents, for example, lower alcohols such as methanol, ethanol, isopropanol and n-butanol, polyhydric alcohols such as propylene glycol and 1,3-butylene glycol, acetone, ethyl acetate ester, etc. When a lower alcohol is used, the resultant extract can be used as such, but it is also possible to distil off the extracting solvent and incorporate the residue, if necessary after being dried, to give a composition for the head of the invention.

[0022] The extract according to the invention can be a treated product at each stage, in accordance with the object, obtained by further subjecting an extract obtained using the above extracting solvent to liquid-liquid distribution with a system comprising a hydrophobic solvent (e.g., n-hexane) and water, extracting the aqueous layer, for example, with ethyl acetate or the like, and then subjecting the extract or the above aqueous layer without the extraction to a suitable column chromatography treatment for separation or the like.

[0023] The compounding amount of the extract according to the invention into the composition for the head is not specified because it can vary depending on the forms or use methods of the composition. However, when such an extract as obtained according to the method described in the later-described examples is used, the compounding amount based on the whole weight of the composition is generally 0.0005 to 20.0 % by weight, preferably 0.001 to 10.0 % by weight in terms of dried matter. When it is more than 20.0 % by weight, formulation is difficult, which is undesirable. Further, even if it is compounded in an amount of more than 10.0 % by weight, so much increase of effect cannot be obtained.

[0035] Namely, the mice were divided into 4 groups for Test samples 1 to 3 and Control sample, each group consisting of 10 animals. The back of each mouse was shaved by hair clippers and a shaver, and each sample was applied in 0.1 ml portions once a day. 18 days and 24 days thereafter, the area where hair was regenerated was measured. The results were expressed as an average value of the regenerated areas. The results are shown in Table 1.

Table 1

Sample	Hair regeneration area (%)	
	18 days later	24 days later
Sample 1 ( <u>Croton birmanicus</u> extract 0.5 %)	76	96
Sample 1 ( <u>Croton birmanicus</u> extract 1 %)	87	100
Sample 1 ( <u>Croton birmanicus</u> extract 2 %)	92	100
Control sample	37	66

[0036] As apparent from Table 1, the Croton birmanicus extract of the invention showed excellent hair generating effect in the murine hair generation test. 2. Other preparation examples

[0037] A methanol extract obtained in the same manner as in Preparation example 1 (299.2 g) (dry weight) was subjected to liquid-liquid distribution between n-hexane (6 L) and water (3 L) to give 51.83 g of dried matter from the n-hexane layer and give the aqueous layer. The aqueous layer was subjected to liquid-liquid distribution between it and ethyl acetate (10 L), and 52.7 g of dried matter was obtained from the ethyl acetate layer (hereinafter, referred to as ethyl acetate fraction).

[0038] The ethyl acetate fraction was fractionated through silica gel column (packing material: Wakogel C-200: 1 kg, eluent; chloroform:methanol = 50:1 → 30:1 → 20:1 → 9:1 → 2:1), the resultant fractions on which C3H mouse hair generating effect was detected were further fractionated by ODS gel column chromatography (ODS gel: 300 g, eluent; 70% methanol → 90% methanol → 100% methanol), and 1.10 g of dried matter was obtained from the middle-stage eluate fractions on which C3H mouse hair generating effect was detected. This was fractionated through silica gel column (packing material: Wakogel C-200: 170 g, eluent; chloroform:methanol = 20:1 → 10:1 → 5:1 → 2:1 → 1:1 → 0:1) From the initial-stage eluate fraction to about 2/5 eluate fraction was obtained 520 mg of dried matter (hereinafter, referred to as Fraction A), and from the 3/5 eluate fraction was obtained 530 mg of dried matter (hereinafter, referred to as Fraction B).

[0039] HPLC was carried out under the following conditions on Fraction A and Fraction B obtained above and 4 $\alpha$ -TPA (comparison). The resultant elution patterns of the respective components are shown in comparison in Fig. 1. A-C.

HPLC conditions

[0040]

#### Mobile phase

0-50 minutes: 80% acetonitrile

50-60 minutes: 80 → 100% acetonitrile

60-80 minutes: 100% acetonitrile

#### Column

Capcell Pak C18 UG120 Å

#### Detection

UV 238 nm

[0041] These samples were subjected to the above hair generation test, and further, stimulation was observed on the skin of the back parts of C3H/HeNCrJ mice which were shaved and coated with the samples. This stimulation means desquamation and acanthosis, and when these are remarkably observed, the expression of ++ is made. when

Table 3

Sample	Rate of hair roots at the telogen			Evaluation of hair revitalizing effect
	20% or more decrease	±20%	20% or more increase	
Sample 4 (0.5%)	59	33	10	effective
Sample 5 (1%)	72	32	1	remarkably effective
Sample 6 (2%)	80	20	0	remarkably effective
Control sample	9	31	59	noneffective

[0050] As apparent from Table 3, the Croton birmanicus extract of the invention showed a significant hair growing effect in the human trichogram test.

### ③ Cell proliferation test using cultured hair dermal papilla cells

#### 1. Preparation of extract

[0051] The preparation of the above extract was carried out by the method of Preparation method 1 in the above hair generation test. Further, the dried methanol extract was made into a 0.2% by weight solution with DMSO, and this was diluted with a serum-free medium (MEM) to give solutions containing the Croton birmanicus extract in concentrations of  $1.0^{-9}$  to  $1.0 \times 10^{-6}$  % (Preparation examples 2 to 5).

#### 2. Collection of hair dermal papilla cells

[0052] The fatty tissue was separated from the skin (5 mm x 1.5 cm) at the occipital region of head of 32-year-old male extirpated by art orthopedic operation, hair follicles were extirpated therefrom, and hair dermal papilla cells were isolated from the hair bulb part. The isolated hair dermal papilla cells were cultured for 2 weeks [37°C, 5% CO<sub>2</sub>] in MEM containing 20% FBS. At the time when the outgrowth of cells from the hair dermal papilla cells was confirmed, the medium was replaced with MEM containing 10% FBS (MEM + 10% FBS), and culturing was carried out under the same conditions. Thereafter, the medium was replaced with MEM + 10% FBS at a rate of twice a week to maintain the cells.

[0053] 4 weeks after the start of culturing, subculturing was carried out, and thereafter, at the time when the cells sufficiently proliferated, subculturing was carried out again, and this passage was repeated.

#### 3. Test method

[0054] A cell suspension having a cell density of 10,000 cells/ml was prepared using hair dermal papilla cells of passage number 3 and MEM+10% FBS medium. 200  $\mu$ l portions of this cell suspension were put in a 96-well microplate (namely, 2,000 cells/well), and incubation was carried out at 37°C and 5% CO<sub>2</sub> for 3 days to let the cells adhere. 72 Hours after the start of culturing, the culture broth for control was replaced with serum-free MEM, and the culture broths for test sample systems were replaced with serum-free media (MEM) containing the Croton birmanicus extract (Preparation examples 2 to 5) (Samples 7 to 10).

[0055] The control and test sample systems were cultured for further 4 days.

[0056] After the completion of culturing, 20  $\mu$ l of alamar blue (made by BIOSOURCE) was added to each system, culturing was carried out for further 8 hours, and absorbance was measured at 570 nm and 595 nm by Micro plate reader (made by BIO RAD). According to the attached operation manual, the reduction rate of alamar blue was calculated based on the measurement results of absorbance. Since this reduction rate correlates with cell number, the cell proliferation rates in the control and test sample systems were compared.

#### 4. Results

[0057] The cell proliferation acceleration indexes in the measured Croton birmanicus extracts (Samples 7 to 10) are shown in the following Table 4.

[0068] 5 ml of PBS (-) containing 0.25% trypsin was added to the hair follicles obtained by the above operations, and the cell suspension was incubated at 37°C for 5 minutes.

[0069] After completion of the incubation, 5 ml of fetal bovine serum (FBS) and 5 ml of Ham's F12 medium were added, the cell suspension was filtered by Cell Strainer (100  $\mu$ m, made by NALGENE) and put in a 50-ml centrifugation tube, and the cell suspension was centrifuged (4°C, 1,500 rpm, 5 minutes). The supernatant was removed from the system, and desired hair follicular epitheliocytes were obtained as the residue.

## 2. Preculturing of the hair follicular epitheliocytes

[0070] In order to remove as many fibroblasts as possible contaminating the system, preculturing of the hair follicular epitheliocytes obtained by the above step was carried out. The procedure is described below.

[0071] The freeze-dried cells obtained in the above step were thawed out in a constant temperature vessel of 37°C. Then, 10 ml of FAD medium [a medium obtained by mixing Ham's F12 medium (described later) and MEN medium in a volume ratio of 3:1 and adding insulin (5.0  $\mu$ g/ml), hydrocortisone (0.45  $\mu$ g/ml), epidermal growth factor (EGF) (10.0 ng/ml), cholera toxin ( $10^{-9}$  M) and fetal bovine serum (10%), this is the same hereinafter) was added to dilute the cell solution, and the system was subjected to centrifugation (10°C or less, 1,500 rpm, 5 minutes). After the centrifugation, the supernatant was removed, 10 ml of FAD medium was added to the system, and pipetting was repeated until the cellular masses disappeared.

[0072] The number of the obtained cells was calculated by a cytometer, and the cell concentration was adjusted to  $2.5 \times 10^5$  cells/ml with FAD medium,

[0073] The cells were spread in a 75 cm<sup>3</sup>-flask coated with I-type collagen, and they were cultured overnight at 37°C and 5% CO<sub>2</sub>.

[0074] After the culturing, the system was washed twice with 10 ml of PBS (-), 2 ml of PBS (-) containing 0.25% trypsin was added, and the mixture was incubated at 37°C and 5% CO<sub>2</sub> for 4 minutes. Then, 2 ml of fetal bovine serum (FBS) was added to the system, the mixture was once gently shaken, and the supernatant was removed to remove the fibroblasts contaminating the system.

[0075] Further, 15 ml of KGK medium [Keratinocyto growth medium: a medium obtained by adding bovine pituitary extract (BPE) (0.4 % by volume), insulin (0.5  $\mu$ g/ml), hydrocortisone (0.5  $\mu$ g/ml) and h-EGF (0.1 ng/ml) to KGM medium (modified MCDB153 medium (made by CLONETICS)), this is the same hereinafter] was added to the system, and the mixture was cultured at 37°C and 5% CO<sub>2</sub> for 3 days.

[0076] The fibroblasts contamination rate (FB contamination rate) of a culturing flask in which the hair follicular epitheliocytes obtained by the above step were spread was measured (3,000 magnifications, 5 visual fields), and the cells having a FB contamination rate of 3% or more were excluded from the subjects of the assay.

[0077] The system was washed twice with 10 ml of PBS (-), 2 ml of PBS (-) containing 0.25% trypsin was added, and incubation was carried out at 37°C for 3 minutes. Then, in order to remove fibroblasts from the system utilizing difference in reactivity with trypsin between epitheliocytes and fibroblasts, trypsin was removed. 2 ml of PBS (-) containing 0.25% trypsin was added again, and the mixture was shaken at 37°C and 20 rpm for 5 minutes.

[0078] Then, peeling of the cells was confirmed under a microscope, 10 ml of DMEM medium containing 10% FBS was added, pipetting was carried out in a 50-ml centrifugal tube, and the system was subjected to centrifugation at 1,500 rpm for 5 minutes.

[0079] The supernatant was removed, 20 ml of KGM medium was added, and pipetting was carried out until the cellular masses disappeared.

[0080] The suspension was filtered by Cell Strainer (100  $\mu$ m, made by NALGENE), and put in a 50-ml centrifugation tube. The number of live cells in the suspension was calculated by a cytometer, and KGM medium was added to the system to adjust the cell concentration in the system to  $5.0 \times 10^4$  cells/ml.

[0081] Then, the cell suspension was spread on a 96-well plate (plate coated with I-type collagen: made by FALCON) at a rate of 0.2 ml/well ( $1.0 \times 10^4$  cells/well), and the system was left alone at room temperature for about 20 minutes until the cells sank on the bottom of the wells.

[0082] Thereafter, culturing was carried out at 37°C and 5% CO<sub>2</sub> for one day to give desired human cultured hair follicular epitheliocytes.

## 3. Preparation of test media

[0083] 0.2% DMSO solution of the methanol extract (dried matter) of *Croton birmanicus* obtained in the above Preparation 1 was added to 1,000 volumes of modified MCDB153 medium (made by CLONETICS) [extract concentration:  $2.0 \times 10^{-4}$  % (DMSO 0.1%)].

[0084] These media to which the target substance was added were added to KBM medium containing 0.1% DMSO to dilute the concentration of the target substance so as to be  $1.0 \times 10^{-8}$  to  $1.0 \times 10^{-5}$  % (Samples 11 to 14). Likewise,

[0092] The effects of the hair tonic prepared in the above formulation in actual use on symptoms such as dandruff, hair generation and alopecia were examined. The hair tonic was administered to 10 males (age 25-55) showing symptoms such as dandruff, hair generation and alopecia, once or twice a day, 1 to 3 ml per each administration, over a period of 4 months, and it was tested for dandruff preventing effect, hair generation accelerating effect and alopecia preventing effect, according to the following criteria. The results are shown in Table 6.

Evaluation criteria

[0093]

(1) Dandruff preventing effect test

Noneffective:

No improvement was observed in spite of the treatment.

Effective:

Generation of dandruff was decreased.

Remarkably effective:

Generation of dandruff was stopped.

(2) Hair generating effect test

Noneffective:

No improvement was observed in spite of the treatment.

Effective:

Generation of hair was observed in 2/3 or more of the alopecia part.

Remarkably effective:

Hair comes out on the whole alopecia part.

(3) Alopecia effect test

Noneffective:

No improvement was observed in spite of the treatment.

Effective:

Progress of alopecia decreased.

Remarkably effective:

Alopecia was stopped.

Table 6

Subject	Age	Dandruff	Hair generation	Alopecia
1	43	remarkably effective	effective	effective



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(continued)

<u>Croton birmanicus</u> extract (Preparation example 1)	0.5
1,3-butylene glycol	5.0
Antiseptic	appropriate amount
Purified water	balance

## Example 3 Hair tonic

[0098]

<u>Croton birmanicus</u> extract (Preparation example 1)	1.0
Stearyltrimethylamine oxid	0.5
Hardened castor oil ethylene oxide (40 mol) adduct	1.0
95% Ethanol	54.0
Deionized water	balance

(Preparation process)

[0099] Deionized water was added to 95% ethanol, then hardened castor oil ethylene oxide (40 mol) adduct and stearyltrimethylamine oxide were added thereto, the dried extract was added, and the mixture was stirred to give a solution.

## Example 4 Hair tonic

[0100]

Glycerol	2.0
L-menthol	0.1
<u>Croton birmanicus</u> extract (Preparation example 1)	2.0
95% Ethanol	54.0
Perfum	0.5
Deionized water	balance

(Preparation process)

[0101] Glycerol, L-menthol, perfume and the dried extract were added to 95% ethanol, the mixture was stirred to give a solution, and deionized water was added.

## Example 5 Hair tonic

[0102]

Sodium N-cocolauryl- $\beta$ -aminopropionat	0.2
--	-----

## Example 8 Hair tonic

[0107]

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Hinokitiol	0.1
<u>Swertia</u> Herb extract	1.0
Vitamin B6	0.2
Vitamin	0.01
Menthol	0.2
Salicylic acid	0.1
<u>Croton birmanicus</u> extract (Preparation example 1)	1.0
Surfactant	0.1
Propylene glycol	2.0
70% Ethanol	balance

## Claims

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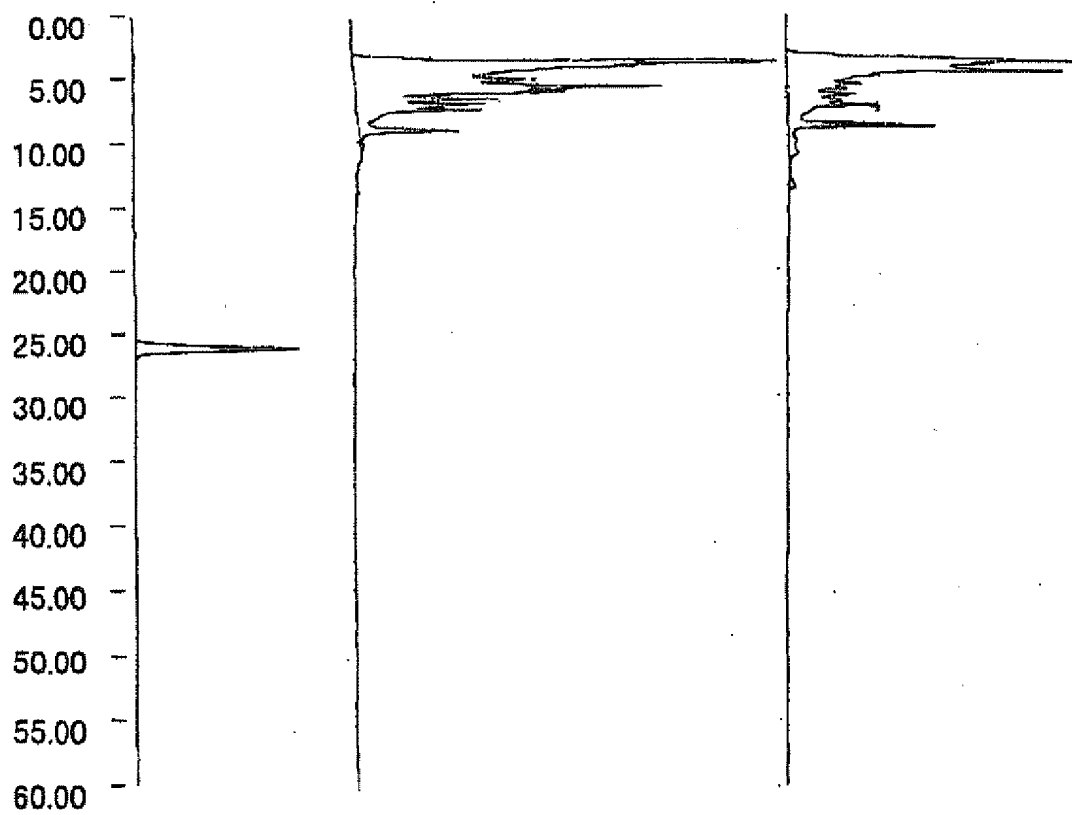
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1. A hair-revitalizing composition comprising an extract from a plant being classified as the genus Croton of the family Euphorbiaceae in an amount effective for revitalization of human hair, and cosmetically or dermatologically acceptable other additives.
2. The hair-revitalizing composition according to claim 1 wherein the plant being classified as the genus Croton is Croton birmanicus Muell. Arg.
3. The hair-revitalizing composition according to claim 1 wherein the extract is an extract obtained by carrying out the extraction using one or two or more selected from the group consisting of water-miscible organic solvents.
4. A composition for activating hair dermal papilla cells of human hair comprising an extract from a plant being classified as the genus Croton of the family Euphorbiaceae in an amount effective for activating the hair dermal papilla cells, and cosmetically or dermatologically acceptable other additives.
5. The composition according to claim 4 wherein the plant being classified as the genus Croton is Croton birmanicus Muell. Arg.
6. A composition for lengthen the anagen in the hair cycle of human hair comprising an extract from a plant being classified as the genus Croton of the family Euphorbiaceae in an amount effective for lengthen the anagen, and cosmetically or dermatologically acceptable other additives.
7. The composition according to claim 6 wherein the plant being classified as the genus Croton is Croton birmanicus Muell. Arg.
8. Use of an extract from a plant being classified as the genus Croton of the family Euphorbiaceae as an effective ingredient, for preparation of hair revitalizing compositions.
9. Use of an extract from a plant being classified as the genus Croton of the family Euphorbiaceae as an effective ingredient, for preparation of compositions activating hair dermal papilla cells of human hair, or lengthening the anagen in the hair cycle.
10. The use according to claim 8 or 9 wherein the plant being classified as the genus Croton is Croton birmanicus Muell. Arg.

FIG.1.A

FIG.1.B

FIG.1.C



**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A61K 7/06, 7/11</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 99/15135</b> <b>(43) International Publication Date:</b> 1 April 1999 (01.04.99)
<b>(21) International Application Number:</b> PCT/IB98/01384 <b>(22) International Filing Date:</b> 7 September 1998 (07.09.98)  <b>(30) Priority Data:</b> 08/937,637 25 September 1997 (25.09.97) US  <b>(71) Applicant:</b> THE PROCTER & GAMBLE COMPANY [US/US]; One Procter & Gamble Plaza, Cincinnati, OH 45202 (US).  <b>(72) Inventors:</b> FOX, Mary, Mora; 7201 Striker Road, Maineville, OH 45039 (US). WOLSING, Dana, Hance; 15344 Parkers Grove, Morning View, KY 41063 (US).  <b>(74) Agents:</b> REED, T., David et al.; The Procter & Gamble Company, 5299 Spring Grove Avenue, Cincinnati, OH 45217-1087 (US).		<b>(81) Designated States:</b> BR, CN, JP, MX, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> HAIR STYLING COMPOSITIONS  <b>(57) Abstract</b>  The present invention relates to hair styling compositions comprising water soluble, non-polymeric mineral salts and lipophilic materials which provide improved hair styling. Specifically, the present invention relates to hair styling compositions comprising water soluble, non-polymeric mineral salts and lipophilic materials further comprising low levels of a dispersing surfactant for improved hair styling.		

## HAIR STYLING COMPOSITIONS

### TECHNICAL FIELD

The present invention relates to hair styling compositions comprising water soluble, non-polymeric mineral salts and lipophilic materials which provide improved hair styling. Specifically, the present invention relates to hair styling compositions comprising water soluble, non-polymeric mineral salts and lipophilic materials further comprising low levels of a dispersing surfactant for improved hair styling.

### BACKGROUND OF THE INVENTION

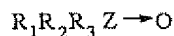
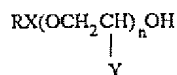
Hair styling compositions, such as hair sprays, styling gels, spray-on gels, and mousses are used on hair to hold the hair in a particularly desired shape or arrangement. A hair arrangement having improved lift, volume and fullness is often a desirable attribute, particularly among consumers with fine, limp or less voluminous hair. Conventional volumizing products generally provide such lift, fullness, control and styling by using fixative resins and polymers. However, these products can be perceived as imparting to hair a stiff, tacky, sticky type of texture, leaving the hair feeling overly coated and rough to the touch.

Chemical processing such as perming, bleaching, highlighting, coloring, and straightening is also a means whereby fullness and volume can be imparted to hair. However, styles typically controlled using such methods are not easily changeable and are frequently time consuming and labor intensive. Moreover, the chemicals employed in such methods can be caustic and somewhat damaging to hair when used excessively.

Mineral salts have been known to be useful as a means of increasing the viscosity of formulations and emulsions when combined with surfactants as disclosed in Encyclopedia of Shampoo Ingredients (A.L.L. Hunting, Micelle Press, 1983). Encyclopedia of Conditioning Rinse Ingredients (A.L.L. Hunting, Micelle Press, 1987).

Compositions containing water soluble, non-polymeric mineral salts have also been described as styling aids. For example, German Patent, DE 2,608,649 to Schulz discloses fat (oil) free compositions which incorporate water soluble, non-polymeric mineral salts to provide a lighter, looser setting of the hair.

nonionic surfactant has a formula selected from the group consisting of:



and mixtures thereof where R is a long chain alkyl group or mixer of alkyl groups containing 10-24 carbon atoms; X is a phenyl,  $\text{>C=O}$ , sulfur or nil; Y is a hydrogen or methyl; and n is an integer from 1 to 20, preferably from 2 to 15, and most preferably from 2 to 10; when X is nil, R is bonded directly to  $-(\text{OCH}_2\text{CH})_n-$  and wherein  $\text{R}_1$  contains an alkyl, alkenyl or monohydroxy alkyl radical of from about 8 to about 18 carbon atoms, from 0 to about 10 ethylene oxide moieties, and from 0 to about 1 glyceryl moiety, and  $\text{R}_2$  and  $\text{R}_3$  contain from about 1 to about 3 carbon atoms and from 0 to about 1 hydroxy group; and Z is a nitrogen, phosphorus or sulfur bonded directly to O;

and

d.) water

wherein the composition contains less than 0.01% cationic surfactant and wherein the composition contains less than about 0.2% by weight of the composition of a chemical protein modifying agent and wherein the composition contains less than 0.01% formate, sorbate, salicylate and carbonate and wherein the composition contains less than about 0.2% of a polymer having a solubility parameter of from about 8.5 to about 12.0  $(\text{cal}/\text{cm}^3)^{1/2}$  and wherein the composition has a hair friction index of at least 1.07.

The present invention further relates to methods of using the hair styling compositions.

#### DETAILED DESCRIPTION OF THE INVENTION

The hair styling compositions of the present invention can comprise, consist of, or consist essentially of the essential elements and limitations of the invention described herein, as well any of the additional or optional ingredients, components, or limitations described herein.

All percentages, parts and ratios are based upon the total weight of the personal cleansing compositions of the present invention, unless otherwise

The compositions of the present invention contain less than about 0.2% of a polymer having a solubility parameter of between about 8.5 to about 12.0  $(\text{cal}/\text{cm}^3)^{1/2}$ . The solubility parameter is defined in the Polymer Handbook 3<sup>rd</sup> ed. (John Wiley and Sons, New York), J. Brandrup and E. H. Immergut, Chapter VII, pp. 519-559 as the square root of the cohesive energy density and describes the attractive strength between molecules of the material. Solubility parameters may be determined by direct measurement, correlations with other physical properties, or indirect calculation. The solubility parameters of polymers can be determined by indirect calculations of group contributions as described in section 2.3 on p. 524-526 of the cited reference.

The hair styling compositions of the present invention, including the essential and optional components thereof, are described in detail hereinafter.

#### Essential Components

##### Water Soluble, Non-Polymeric Mineral Salt

An essential component of the hair styling compositions of the present invention is a friction enhancing agent which is a water soluble, non-polymeric mineral salt. By the term "non-polymeric", as used herein means the mineral salts of the present invention comprise no molecules comprising non repeating moieties units (monomers). Without being limited by theory, it is believed that when the water soluble, non-polymeric mineral salt is solubilized and the resultant solution applied to (and dried on) the hair, the water soluble salt begins to precipitate onto the surface of the dry hair, increasing the hair's overall surface friction, thus improving styling volume and fullness. Suitable water soluble, non-polymeric mineral salts include naturally occurring or synthetically derived, anhydrous and hydrate forms of mono-, di- and trivalent inorganic salts as well as organic salts. Surfactant salts and salt polymers themselves are not included in the present electrolyte definition but other salts are. Suitable anionic salt substituents include, but are not limited to, halides, carbonates, phosphates, sulfates, nitrates, citrates, malates, gluconates, lactates, maleates, succinates, acetates, benzoates, fumerates and the like. The counter ions of such anionic substituents are metal ions and can be, but are not limited to, magnesium, calcium, sodium, potassium, or other mono- and divalent cations. Electrolytes most preferred for use in the compositions of the present invention include sodium, potassium and magnesium sulfates; sodium and potassium hydrogen carbonates or hydrogen sulfates; sodium and potassium carbonates; sodium, potassium, magnesium and calcium primary phosphates as well as sodium and potassium secondary phosphates. It is recognized that these salts may serve as thickening aids or buffering aids in

perfumery uses, including materials such as aldehydes, ketones, esters and the like. More commonly, naturally occurring plant and animal oils and exudates comprising complex mixtures of various chemical components are known for use as perfumes, and such materials can be used herein. Perfumes suitable for use in the compositions of the present invention are described in U.S. Patent 5,676,584 (Angell et. al.) and further disclosed in S. Arctander, Perfume Flavors and Chemicals, Vols. I and II, Author, Montclair, N.J., and the Merck Index, 12th Edition, Merck & Co., Inc. Rahway, N.J., all of which are herein incorporated by reference in their entirety.

Non limiting examples of oil-soluble vitamins such vitamins A, vitamins D, vitamins E, vitamins K, and ubiquinones are found in U.S. Patent 5,489,303 (Saski et. al.), herein incorporated by reference in its entirety.

The lipophilic materials of the present invention also include essential oils. Examples of suitable essential oils are found in U.S. Patent 5,665,689 (Durbut), herein incorporated by reference in its entirety.

Mixtures of the above lipophilic materials may also be used. The lipophilic materials of the present invention are preferably present at concentration levels of from about 0.05% to about 0.5%, preferably from about 0.05% to about 0.3%, most preferably from about 0.05% to about 0.2%.

#### Surfactant

The hair styling compositions of the present invention also require a surfactant. Preferably the surfactants of the present invention are water soluble surfactants. By "water-soluble surfactant" is meant surfactant materials which form clear solutions when dissolved in water at 0.2 weight percent at ambient conditions. For the purposes of the present invention, the term "clear" is intended to mean that the solution formed is substantially transparent to visible light although a slight amount of haze may be present as long as one can see through the composition. Surfactants suitable for use in the present compositions include anionic surfactants, amphoteric surfactants and mixtures thereof as well as nonionic surfactants, cationic surfactants or mixtures thereof. Amphoteric surfactants useful in the present composition include those known to be useful in cosmetic compositions, and which, preferably, contain a group that is anionic at the pH of the compositions of the present invention.

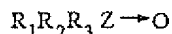
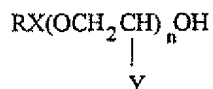
Examples of amphoteric surfactants suitable for use in the compositions are described in U.S. Patent 4,472,297 (Bolich Jr. et. al.); U.S. Patent 5,104,646 (Bolich Jr. et. al.); and U.S. Patent 5,106,609 (Bolich Jr. et. al.) and can be further described in "Surfactant Science Series: Amphoteric Surfactants", Volume



alkaline metal; and mixtures thereof. More preferably, the alkyl radicals, R in the above formulas, are saturated and straight chain.

The AGS surfactants useful in the present invention are more fully described in U.S. Patent No. 2,979,465, to Parran et. al., issued April 11, 1961; U.S. Patent No. 3,179,599, to Eaton et. al., issued April 20, 1965; British Patent No. 848,224, published Sept. 14, 1960; British Patent No. 791,415, published March 5, 1958; U.S. Patent No. 5,322,643, to Schwartz et. al., issued June 21, 1994; and U.S. Patent No. 5,084,212, to Farris et. al. issued Jan. 28, 1992; which are all hereby incorporated herein by reference in their entirety. These references also disclose various cleansing products in which the AGS surfactant of this invention can be used. Mixtures of any of the above described anionic surfactants can be used in the composition of the present invention.

The surfactant component of the present invention may also include nonionic surfactants. Nonionic surfactants suitable for use in the compositions of the present invention have a formula selected from the group consisting of:



and mixtures thereof where R is a long chain alkyl group or mixer of alkyl groups containing 10-24 carbon atoms; X is a phenyl,  $\text{>C=O}$ , sulfur or nil; Y is a hydrogen or methyl; and n is an integer from 1 to 20, preferably from 2 to 15, and most preferably from 2 to 10; when X is nil, R is bonded directly to  $-(\text{OCH}_2\text{CH})_n-$  and wherein R<sub>1</sub> contains an alkyl, alkenyl or monohydroxy alkyl radical of from about 8 to about 18 carbon atoms, from 0 to about 10 ethylene oxide moieties, and from 0 to about 1 glyceryl moiety, and R<sub>2</sub> and R<sub>3</sub> contain from about 1 to about 3 carbon atoms and from 0 to about 1 hydroxy group, e.g., methyl, ethyl, propyl, hydroxymethyl, hydroxyethyl, or hydroxypropyl radicals; where Z is a nitrogen, phosphorus or sulfur bonded directly to O (oxygen). The arrow in the formula is a conventional representation of a semipolar bond.

Nonionic surfactants suitable for use in the present compositions are described in U.S. Patent 4,472,297 (previously incorporated by reference) and are further described in "Surfactant Science Series: Nonionic Surfactants", Volume 1, edited by Martin J. Schick, Marcel Dekker, New York (1966) all of which are herein incorporated by reference in its entirety. Mixtures of any of the above

#### Additional Friction Enhancing Agent

The hair styling compositions of the present invention preferably contain relatively small amounts of conventional friction enhancing agents. The term "Friction enhancing agents", as used herein means agents which tend to raise the hair friction significantly versus water treated hair, as measured by the KES-SE Friction Test Method described below. Examples of such friction enhancing agents, other than the water soluble, non-polymeric minerals described above, include, but are not limited to natural and synthetic polymers and resins such as polyvinylpyrrolidone/vinyl acetate, polyquaternium-11, polyquaternium-4, butyl ester of polyvinylmethacrylate/methacrylate copolymer; inorganic clays such as bentonite, ceramic, kaolin, slip clays, polyorganosilicates, kaolinite, montmorillonite, atapulgite, illite, bentonite, halloysite, silica, alumina, muds; water insoluble minerals such as calcium carbonate, calcium oxalate, calcium polyphosphates; sawdust; plant polysaccharides; and crustacean shells. Preferably, the additional friction enhancing agents are present at concentration levels of less than about 2%, more preferably about 1.5%.

#### Hair Friction Index Measurement Test

The hair styling compositions of the present invention preferably have a hair friction index of at least about 1.07, preferably 1.10, most preferably 1.15, as measured by the KES-SE Friction Test.

The KES-SE Friction Test Method evaluates the friction force of the surface of a flat hair switch. This is achieved with the use of a Friction instrument, KES-SE Model (by Kato Tech Ltd., Kyoto, Japan). Specific instructions for calibration, instrument operation and instrument care are provided by the manufacturer and are generally known to those of ordinary skill in the art. The hair friction index is determined as follows.

A round glass frit 25 mm in diameter, with a porosity = C is attached to the sensor probe. The probe with the frit is weighed to the nearest 0.01 grams. The weight of the probe with glass frit should be approximately 22 grams. A control group is prepared comprised of four hair switches made up of 8 grams of hair. Each hair switch is then water treated. Water treatment of the control group switches comprises pre-wetting, shampooing and rinsing each hair switch using running water flowing at a flow rate of 1.5 cubic feet per min. Warm water ( $\approx 40^{\circ}\text{C}$ ) is used throughout the treatment process. The hair switches are blotted with a water-absorbing, nonwoven paper material. Approximately 0.1 grams of water per gram of hair switch is then applied uniformly to each hair switch and massaged throughout the hair. The hair switches are dried using a hot air ( $\approx 55^{\circ}$

sampled T-test. A more detailed discussion of the disclosed friction test method is found in "Methods for the Measurement of the Mechanical Properties of Tissue Paper", R.S. Ampuski, Int. Paper Phys. Conf., pp. 19-30 (1991).

#### Thickening Agent

The personal care compositions of the present invention may also comprise a thickener or thickening agent. Such thickening agents typically comprise cationic, nonionic, anionic, and amphoteric polymers. The thickening agent is preferably present at a level of less than about 2%, more preferably from about 0.05% to about 1.5% by weight of the composition.

Polymers suitable for use as thickening agents herein include any polymer soluble or colloidally dispersible in the aqueous phase (if water is the only solvent in the aqueous phase, the polymer should be soluble or dispersible in water; if an optional cosolvent such as ethanol is present the polymer should be soluble or dispersible in the combined solvent system). Solubility/dispersibility is determined at ambient conditions of temperature and pressure (25°C at 1At). Polymers for use in the compositions of the present invention include cationic, anionic, nonionic, and amphoteric resins. Polymeric thickeners useful in the present are described in U.S. Patent 5,100,658 (Bolich, Jr. et. al.), herein incorporated by reference.

Nonlimiting examples of preferred thickening polymers include Polyquaternium-10 (hydroxyethylcellulose hydroxypropyl trimethylammonium chloride ether) under the trade name Ucare LR Polymers and JR Polymers, natural and derivatized polysaccharides which include guar gums, modified guar gums, locust bean gums, carrageenans, alginates, xanthan gums, sodium alginates, sodium carrageenans, plant extracts of acacia, ghatti, and tragacanth, propylene glycol alginate, and carboxymethylcellulose and mixtures thereof.

#### Pharmaceutical Actives

The compositions of the present invention, especially the topical skin care compositions, can comprise a safe and effective amount of a pharmaceutical active. The phrase "safe and effective amount", as used herein, means an amount of an active high enough to significantly or positively modify the condition to be treated, but low enough to avoid serious side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgment. A safe and effective amount of the pharmaceutical active will vary with the specific active, the ability of the composition to penetrate the active through the skin, the amount of composition to be applied, the particular condition being treated, the age and physical condition of

agents. This list of optional components is not meant to be exclusive, and other optional components can be used.

#### Method of Manufacture

The hair styling compositions of the present invention, in general, can be made by simply mixing together all components using low shear mixing methods. In compositions which use thickening agents, it is advantageous to first solubilize the thickening agents in water before the addition of the other components and the water soluble salts of the compositions.

#### Method of Use

The hair styling compositions of the present invention are used in a conventional manner for applying styling products to the hair. An effective amount of the composition for treating the hair is applied to the hair, that has preferably been wetted with water, and then leaving the composition on the hair to dry or aiding in the drying process with hot air blow drier devices or heated implements. Such effective amounts generally range from about 0.5 g to about 50g, preferably from about 1 g to about 20g. Application to the hair typically includes contacting the hair with the composition and working the composition throughout the hair or specifically where the effect is most desired.

This method for treating the hair comprises the steps of:

a) wetting the hair with water, b) applying an effective amount of the hair styling composition to the hair, and c) allowing the composition to dry on hair as the hair dries or is dried with a hot air appliance.

#### Examples

The hair styling compositions illustrated in Examples 1-6 illustrate specific embodiments of the styling compositions of the present invention, but are not intended to be limiting thereof. Other modifications can be undertaken by the skilled artisan without departing from the spirit and scope of this invention. These exemplified embodiments of the hair styling compositions of the present invention provide improved hair styling and conditioning.

All exemplified compositions can be prepared by conventional formulation and mixing techniques. Component amounts are listed as weight percents and exclude minor materials such as diluents, filler, and so forth. The listed formulations, therefore, comprise the listed components and any minor materials associated with such components.

## EXAMPLE 3

The following is an example of a hair lotion incorporating the compositions of the present invention. The compositions are formed by combining and mixing the ingredients of each column using conventional technology and then applying to hair from about from about 0.5 g to about 50g.

LOTION COMPOSITION	% w/w
Xanthan Gum	1.0
Quaternium-15 (Dowicil 200, Dow Chemical, Midland, MI)	0.135
Sodium Benzoate	0.25
Cocamidopropyl betaine (Tegobetaine F-B, Goldschmidt, Hopewell, VA)	0.075
Magnesium Sulfate Heptahydrate	3.08
Perfume	0.06
Citric Acid	0.2
Water	q.s. to 100%

## EXAMPLE 4

The following is an example of a hair spray incorporating the compositions of the present invention. The compositions are formed by combining and mixing the ingredients of each column using conventional technology and then applying to hair from about from about 0.5 g to about 50g.

SPRAY COMPOSITION	% w/w
Xanthan Gum	0.1
Magnesium Sulfate heptahydrate	2.05
Sodium Benzoate	0.25
DMDM Hydantoin (Glydant, Lonza Inc., Fairlawn, NJ)	0.20
Cocamidopropyl betaine (Tegobetaine F-B, Goldschmidt, Hopewell, VA)	0.075
Perfume	0.05
Citric Acid	0.1
Water	q.s. to 100%

## EXAMPLE 6

The following is an example of a foam incorporating the compositions of the present invention. The compositions are formed by combining and mixing the ingredients of each column using conventional technology and then applying to hair from about from about 0.5 g to about 50g.

FOAM COMPOSITION	% w/w
Polyquaternium-10 (U-Care Polymer LR-400, Amerchol, Edison, NJ)	0.25
Sodium Sulfate	1.0
Tetrasodium EDTA	0.13
DMDM Hydantoin (Glydant, Lonza Inc., Fairlawn, NJ)	0.20
Cocamidopropyl betaine (Tegobetaine F-B, Goldschmidt, Hopewell, VA)	0.015
Laureth-4 (Brij 30, ICI Surfactants, Wilmington, DE)	0.004
Sodium Lauroyl Sarcosinate (Hamposyl L-30, Hampshire Chem. Corp., Lexington, MA)	0.07
Perfume	0.05
Citric Acid	0.1
Water	q.s. to 100%

2. A composition according to Claim 1, wherein the water soluble, non-polymeric mineral salt is selected from the group consisting of sodium, potassium, calcium and magnesium salts of sulfate, chloride, gluconate, lactate, acetate, and citrate.
3. A composition according to either of Claim 1 or Claim 2, wherein the anionic surfactant is selected from the group consisting of sulfates, sulphonates, taurines, sarcosinates, and isethionates and mixtures thereof.
4. A composition according to any of the preceding Claims, wherein the amphoteric surfactant is selected from the group consisting of alkylbetaines, alkylamphoacetates and alkyaminopropionates and mixtures thereof.
5. A composition according to any of the preceding Claims, wherein the nonionic surfactant is selected from the group consisting of alkyl polyethyleneglycol ethers, alkyl polypropyleneglycol ethers, alkyl polyethylene glycol esters, and alkyl polypropylene glycol esters and mixtures thereof.
6. A composition according to any of the preceding Claims, wherein the lipophilic material is selected from the group consisting of perfume oils, preservatives, oil-soluble vitamins, oil-soluble pro-vitamins, essential oils and mixtures thereof.
7. A composition according to Claim 6, wherein the preservative is selected from the group consisting benzyl alcohol, methyl paraben, propyl paraben, butyl paraben, isobutyl paraben, isopropyl paraben, and mixtures thereof.
8. A composition according to either of Claim 6 or Claim 7, further comprising a water-soluble preservative selected from the group consisting of DMDM Hydantoin, 1-cis-3-chloroallyl-3-5-7-triaza, methylchloro-isothiazolinone, methyl isothiazolinone, imidazolidinyl urea, sodium benzoate, fatty alcohol quats, phenoxyethanol, EDTA and its salts, and mixtures thereof.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 98/01384

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61K7/06 A61K7/11

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 12787 A (JEYES GROUP PLC) 2 May 1996 see claim 1 see page 6, paragraph 4 see page 7 - page 9 see page 10, paragraph 1 see page 12, paragraph 1 see page 15, paragraph 2	1-6, 10
X	DE 92 10 516 U (KAO) 27 January 1994 see claim 1 see page 2, paragraph 4 see page 3, paragraph 3 see page 4, paragraph 2 see page 6	1, 2, 6, 7, 10, 12-14

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

30 November 1998

Date of mailing of the international search report

04/12/1998

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Authorized officer

Peeters, J



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 98/01384

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9612787 A	02-05-1996	AU 3704195 A AU 4394496 A WO 9621721 A	15-05-1996 31-07-1996 18-07-1996
DE 9210516 U	09-12-1993	NONE	
EP 399157 A	28-11-1990	DE 3916917 A WO 9014070 A JP 4501422 T	29-11-1990 29-11-1990 12-03-1992